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end 244B of the integral cartridge assembly 214 include bayonet threads 280 which are engageable with corresponding groove 282 formed in the distal end of the pen body 212. The distal end 244A of the tubular barrel is configured to securely but releasably engage a needle cannula assembly (not shown).

5

The cartridge assembly 214 shown in Fig. 7 may be assembled and pre-filled by any suitable means, including those disclosed, for example, in U.S. Patent Nos. 5,279,585 (Balkwill), 5,531,255 (Vacca), 5,519,984 (Veussink et al.), 5,373,684 (Vacca), 5,207,983 (Liebert et al.), 4,718,463 (Jurgens, Jr. et al.), and 4,628,969 (Jurgens, Jr. et al.), and PCT Application No. WO 94/13328 (Hagen), the disclosures of which are hereby incorporated by reference in their entirety.

10

Fig. 8 shows yet another alternative embodiment of the cartridge assembly 314 which is disposable and includes single vial retainer 332. However, a stop has been situated in the distal end 338B of the vial retainer 332 which permit the drug cartridge 340 to be inserted into the cavity 334 in one direction but resists removal of the drug cartridge, i.e., the insertion force is less than the removal force. Specifically, protrusions 360 project inwardly and extend along the neck 348 of the drug cartridge 40 to securely retain it in the cartridge assembly. In this way, upon utilization of the medication, the drug cartridge assembly 314 along with the empty drug cartridge 340 may be disengaged from the pen body assembly and safely discarded.

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Fig. 9 shows yet another alternative embodiment of the cartridge assembly 414 which is disposable and includes single vial retainer in which a flexible vial or drug container 440 such as a pouch can be inserted into the cartridge assembly. Attached by threads or the like to the end 438B of the cartridge assembly is a cannula 490 having a double ended needle 492. In this way, upon movement of the plunger or stopper

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454, the proximal end of the needle 492 pierces the drug container to permit the drug to be released therefrom as the container collapses.

The particular material of which the cartridge assembly is made is not essential to the present invention but preferably includes a polymeric material such as polycarbonate. However, the particular material is a matter of choice depending upon availability, the manufacturing process used and the intended use of the cartridge assembly. For example, where the cartridge assembly 214 is pre-filled with the medication, the polymeric material must be compatible with the medication contained therein.

It should be appreciated from the detailed description of the preferred embodiments, that the particular means by which the pen body assembly 12 and the cartridge assembly are keyed, i.e., engaged so as to reduce or otherwise eliminate cross-use is essential and may be threadedly engaged by corresponding threads and grooves, bayonet threads and grooves, snap fits or a pair of lugs that mate in a reverse Luer-lock manner. In this way, the pen body assembly 12 includes either a female or male mating member and the cartridge assembly 14 includes a corresponding female or male mating member engageable with one another for interconnecting the two assemblies, with the mating members selected so as to prevent cross-use with other assemblies, e.g., the pitch of the threads may be angled so as to mate only with one another and not with other assemblies.

Also, the cartridge holder sleeve can have an embedded cartridge, not readily separable from each other as described in connection with one alternative embodiment. In addition, the drug cartridge can be designed as a single integral unit

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for containing the drug as described in connection with another alternative embodiment.

While the preferred embodiments of the present invention have been described  
5 so as to enable one skilled in the art to practice the device of the present invention, it  
is to be understood that variations and modifications may be employed without  
departing from the concept and intent of the present invention as defined in the  
following claims. The preceding description is intended to be exemplary and should  
not be used to limit the scope of the invention. The scope of the invention should be  
10 determined only by reference to the following claims.

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What is claimed is:

1. A disposable, pre-fillable drug cartridge for use with a reusable body assembly of a medication delivery pen, said drug cartridge comprising:
  - 5 a generally tubular barrel having a distal end and an open proximal end, with a chamber defined by a tubular wall of the barrel extending between said distal end and said proximal end;  
sealing means associated with the distal end of said tubular barrel for sealing the distal end of said tubular barrel;
  - 10 plunger means associated with the open proximal end of said tubular barrel in sliding fluid-tight engagement with the tubular wall of the barrel for selective engagement with an advancing member so that distally directed forces on the plunger urge a medication pre-filled in the chamber from the cartridge; and  
mating means for releasably interconnecting said drug cartridge with a pen
  - 15 body assembly and said mating means being associated with the proximal end of said tubular barrel.
2. The drug cartridge of Claim 1, wherein said mating means includes an array of threads on said proximal end of said tubular barrel.
- 20 3. The drug cartridge of Claim 2 wherein said array of threads on the proximal end of said tubular barrel define internal threads in said tubular barrel.
4. The drug cartridge of Claim 1 wherein said distal end of the tubular  
25 barrel is configured to securely but releasably engage a needle cannula assembly.

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5. The drug cartridge of Claim 1 wherein said generally tubular barrel is made of a polymeric material.

6. The drug cartridge of Claim 1 further comprising a medication  
5 contained in said chamber.

7. A disposable, pre-fillable drug cartridge for use with a reusable body assembly of a medication delivery pen, said drug cartridge comprising:

10 a generally tubular barrel made of a polymeric material having a distal end and an open proximal end, with a chamber defined by a tubular wall of the barrel extending between said distal end and said proximal end;

sealing means associated with the distal end of said tubular barrel for sealing the distal end of said tubular barrel;

15 an elastomeric plunger associated with the open proximal end of said barrel in sliding fluid-tight engagement with the tubular wall of the barrel;

medication contained in the chamber and retained therein by the seal and plunger so that distally directed forces on the plunger urge the medication from the cartridge; and

20 mating means for releasably interconnecting said drug cartridge with a pen body assembly and said mating means being associated with the proximal end of said tubular barrel.

8. The drug cartridge of Claim 7, wherein said mating means includes an array of threads on said proximal end of said tubular barrel.

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9. The drug cartridge of Claim 8 wherein said array of threads on the proximal end of said tubular barrel define internal threads in said tubular barrel.

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10. The drug cartridge of Claim 7 wherein said distal end of the tubular barrel is configured to securely but releasably engage a needle cannula assembly.

5 11. The drug cartridge of Claim 7 wherein said medication is contained within a flexible container and a needle cannula attached to distal end of the tubular barrel with said cannula included a double ended needle so that one end of said double ended needle can pierce said flexible container.

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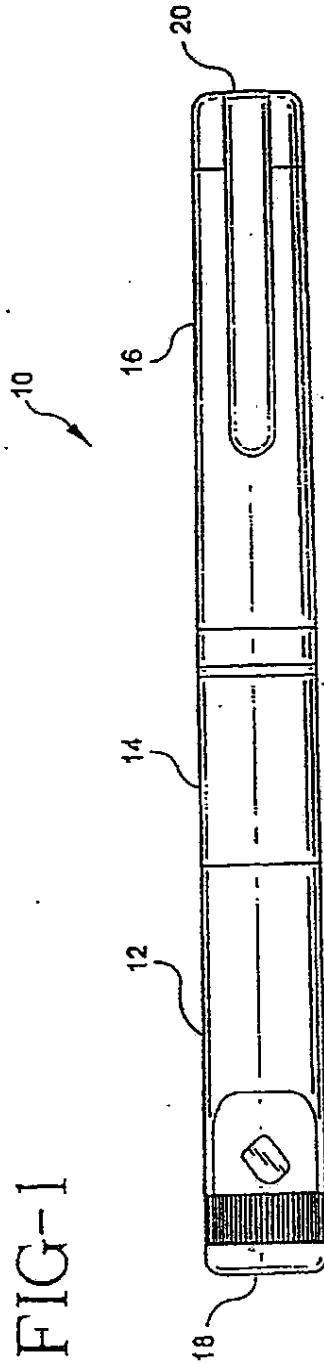


FIG-1A



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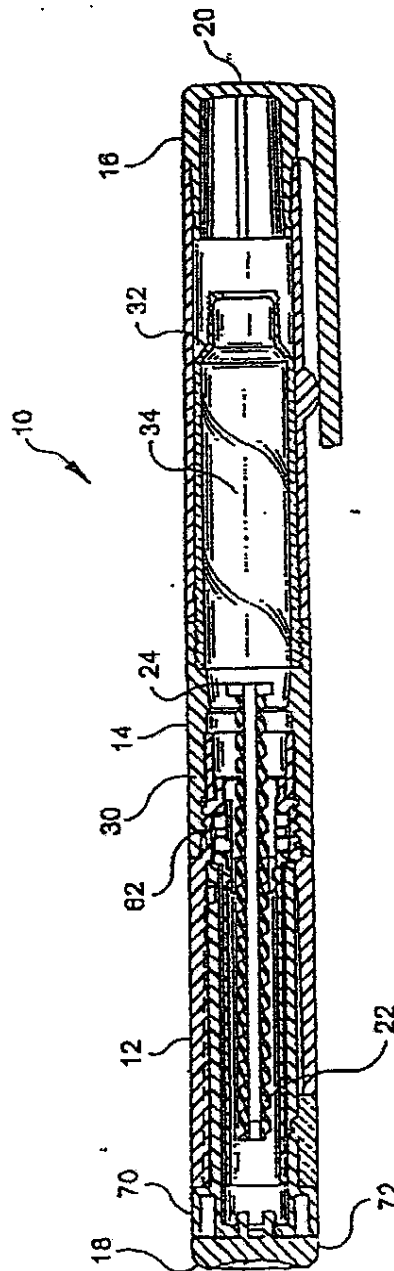
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FIG-2



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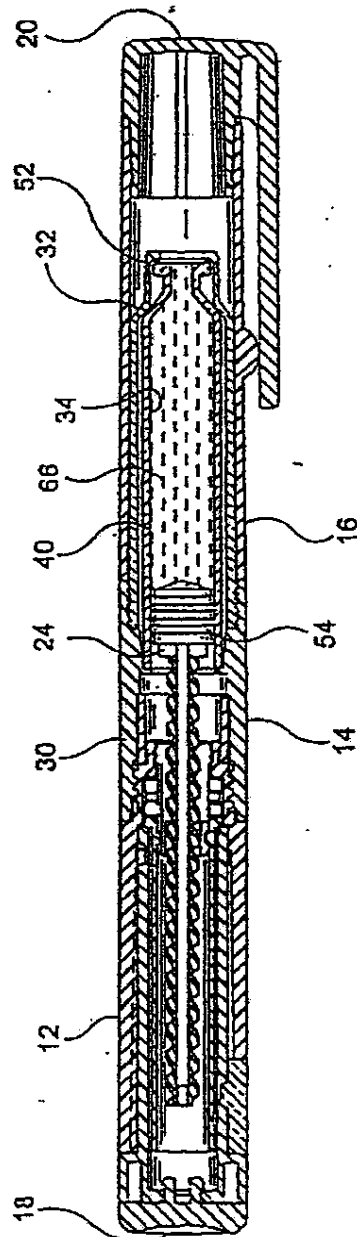
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FIG-3



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FIG-4

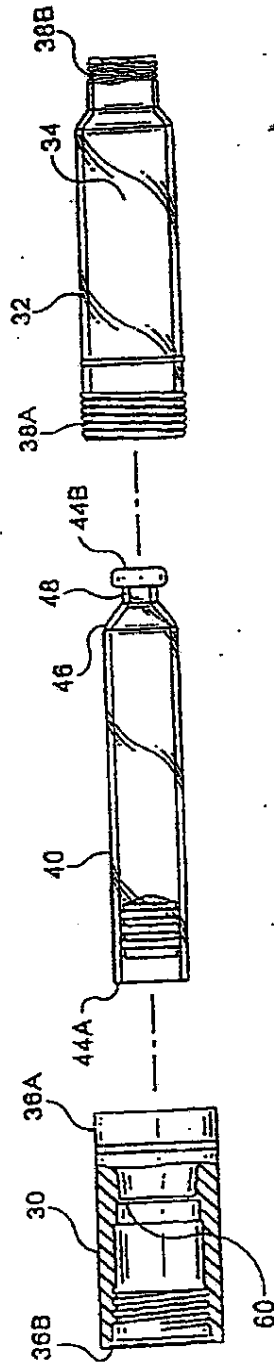
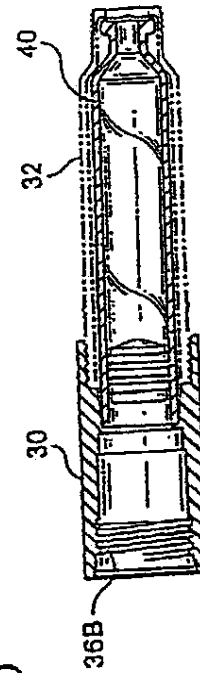


FIG-5



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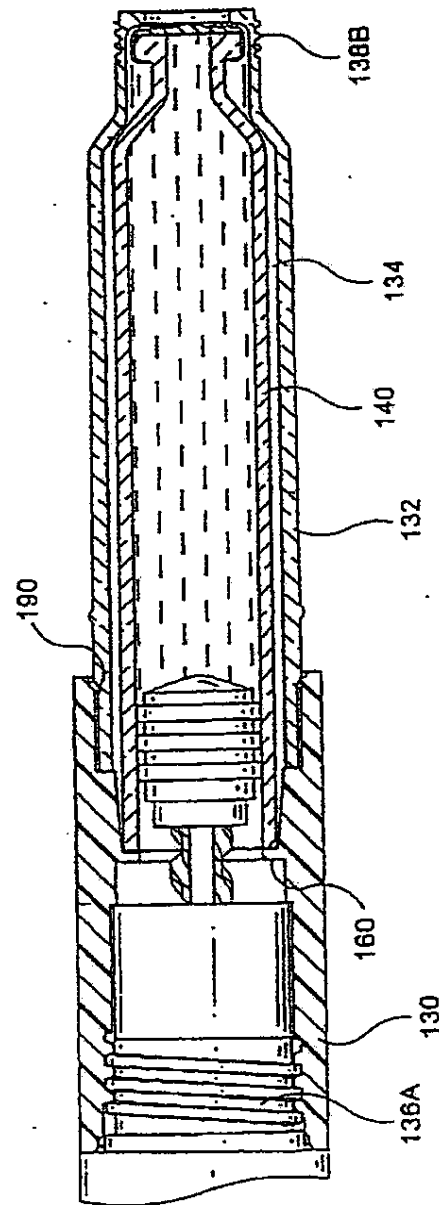
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FIG-6



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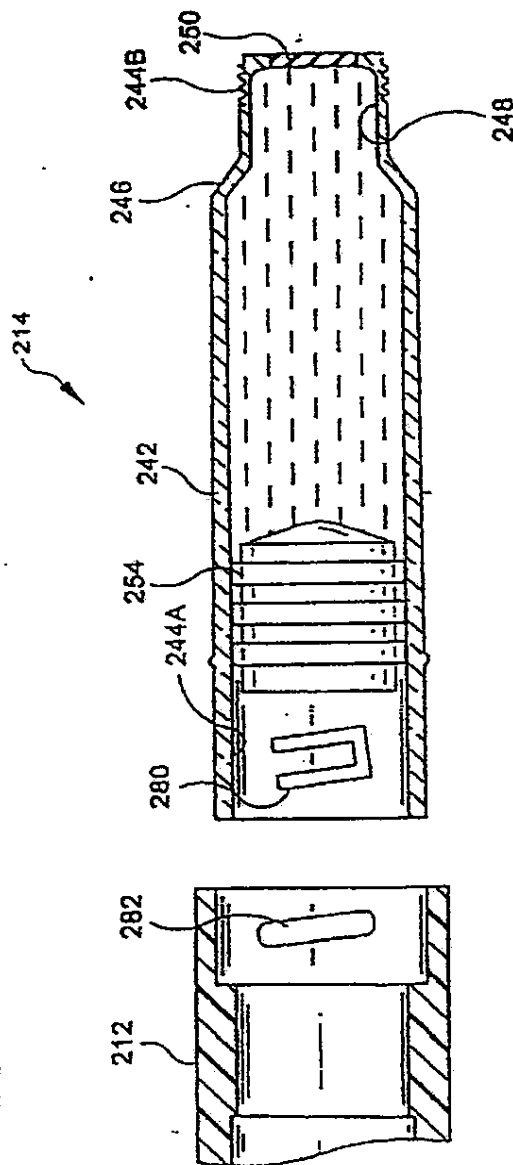
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FIG-7



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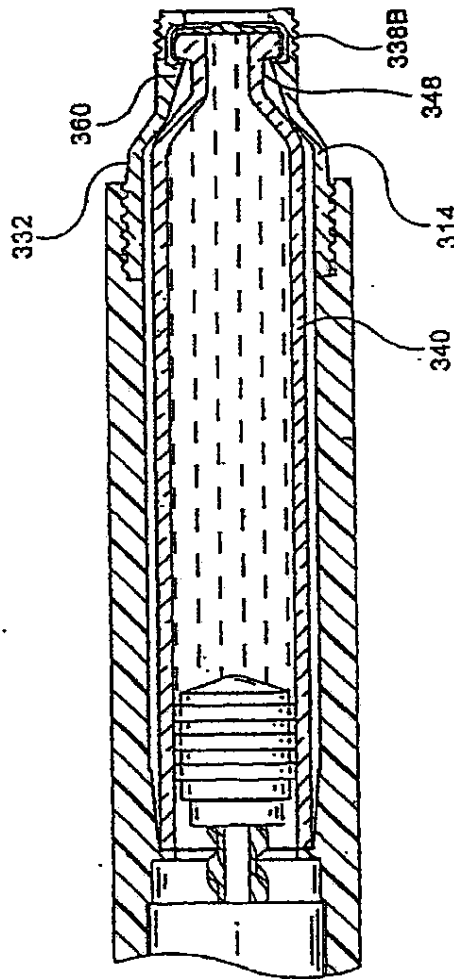


FIG-8

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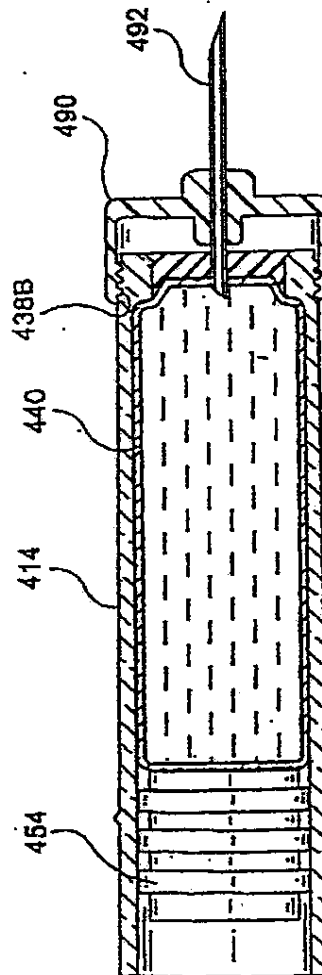
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FIG-9



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## INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/US 98/19649A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61M5/24

According to International Patent Classification (IPC) or to both national classifications and IPC

## B. FIELDS SEARCHED

Mention of document searched (classification system followed by classification symbols)  
IPC 6 A61M

Documentation searched other than citation documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search phase of data base and, where practical, search terms used

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	---	5.7
Y	WO 90 00073 A (BRUNEL) 11 January 1990 see page 4, line 5 - line 6 see page 7, line 11 - line 1 see claim 1; figures 3,6,9	1
A	---	2-4
Y	US 2 685 878 A (SEIFERT ET AL.) 10 August 1954 see column 2, line 11 - line 16 see figures 1.2	8-10
A	---	

☒ Further documents are filed in the continuation of Des C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents

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Date of the actual completion of the international search

12 January 1999

Date of mailing of the international search report

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Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/US 98/19649

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of documents, with indications where appropriate, of the relevant passages	Relevant to Claim No.
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A	EP 0 701 832 A (ELECTON DICKINSON AND COMPANY) 20 March 1996 see column 6, line 21 - line 25 see column 8, line 32 - line 48 see figure 1 see claims 1.10; figure 1 & US 5 558 259 A cited in the application	1.4-7.10

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Form PCT/ISA210 (Continuation of second sheet) June 1992

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Information on patent family members

International Application No.  
PCT/US 95/19649

Patent document class in search report		Publication date	Patent family member(s)	Publication date
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(72) Inventor: Chanock, Lawrence H.  
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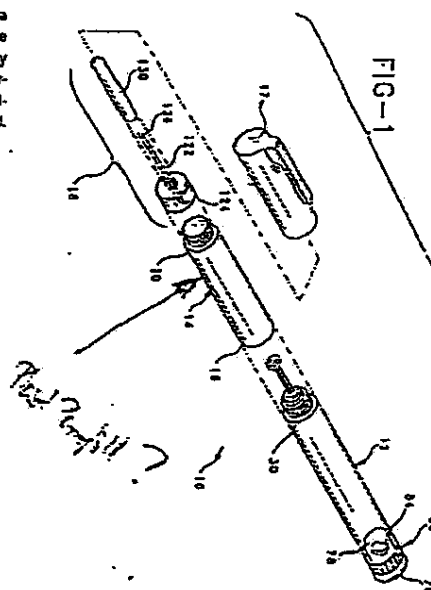
(30) Priority: 19.09.1994 US 308767

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(54) Medication delivery pen with variable increment dose scale

(57) A medication delivery pen is provided having a pen body assembly and a cartridge assembly that are threadably engageable with one another. The pen body assembly includes a rotatable driver for driving a cartridge plunger preselected distances that are in accordance with a desired dose of medication to be delivered. The driver providing different preset rates of injection.



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## Description

BACKGROUND OF THE INVENTION1. Field of the Invention

The subject invention relates to medication delivery pens having a cartridge holder assembly and a pen body assembly removably mounted to the cartridge holder assembly for delivering medication having an improved dose setting device.

2. Description of Related Art

Hypodermic syringes are used to deliver selected doses of medication to patients. The prior art hypodermic syringe includes a syringe barrel having opposed proximal and distal ends. A cylindrical chamber wall extends between the ends and defines a fluid receiving chamber. The proximal end of the prior art syringe barrel is substantially open and receives a plunger in sliding fluid tight engagement. The distal end of the prior art syringe barrel includes a passage communicating with the chamber. A needle cannula is mounted to the distal end of the prior art syringe barrel, such that the lumen of the needle cannula communicates with the passage and the chamber of the syringe barrel. Movement of the plunger in a proximal direction draws fluid through the lumen of the needle cannula and into the chamber. Movement of the plunger in a proximal-to-distal direction urges fluid from the chamber and through the lumen of the needle cannula.

Medication to be injected with the prior art hypodermic syringe often is stored in a vial having a pierceable elastomeric seal. Medication in the prior art vial is accessed by piercing the elastomeric seal with the needle cannula. A selected dose of the medication is drawn into the chamber of the syringe barrel by moving the plunger a selected distance in a proximal direction. The needle cannula is withdrawn from the vial, and the medication is injected into a patient by moving the plunger in a distal direction.

Some medication, such as insulin is self-administered. The typical diabetes patient will require injections of insulin several times during the course of the day. The required dose of insulin will vary from patient to patient, and for each patient may vary during the course of the day and from day to day. Each diabetes patient will establish a regimen that is appropriate for his or her own medical condition and for his or her lifestyle. The regimen typically includes some combination of a slow or medium acting insulin and a faster acting insulin. Each of these regimens may require the diabetes patient to periodically self-administer insulin in public locations, such as places of employment or restaurants. The required manipulation of the standard prior art hypodermic syringe and vial can be inconvenient and embarrassing in these public environments.

Medication delivery pens have been developed to

facilitate the self-administration of medication. One prior art medication delivery pen includes a vial holder into which a vial of insulin or other medication may be received. The vial holder is an elongate generally tubular structure with proximal and distal ends. The distal end of the prior art vial holder includes mounting means for engaging a double-ended needle cannula. The proximal end also includes mounting means for engaging a driver and dose setting apparatus as explained further below. A disposable vial for use with the prior art vial holder includes a distal end having a pierceable elastomeric seal that can be pierced by one end of a double-ended needle cannula. The proximal end of this prior art vial includes a plunger slidably disposed in fluid tight engagement with the cylindrical wall of the vial. This prior art medication delivery pen is used by inserting the vial of medication into the vial holder. A prior art pen body then is connected to the proximal end of the vial holder. The pen body includes a dose setting apparatus for designating a dose of medication to be delivered by the pen and a driving apparatus for urging the plunger of the vial distally for a distance corresponding to the selected dose.

The user of the pen mounts a prior art double-ended needle cannula to the distal end of the vial holder such that the proximal point of the needle cannula pierces the elastomeric seal on the vial. The patient then selects a dose and operates the pen to urge the plunger distally to deliver the selected dose. The dose selecting apparatus returns to zero upon injection of the selected dose with this prior art medication delivery pen. The patient then removes and discards the needle cannula, and keeps the prior art medication delivery pen in a convenient location for the next required medication administration. The medication in the vial will become exhausted after several such administrations of medication. The patient then separates the vial holder from the pen body. The empty vial may then be removed and discarded. A new vial can be inserted into the vial holder, and the vial holder and pen body can be reassembled and used as explained above.

The above described medication delivery pen is effective and much more convenient for self-administration of medication than the typical hypodermic syringe and separate medication vial. However, prior art medication delivery pens are limited to a particular range of dosage amounts because of the fairly complex dosage selecting and driving mechanisms within the delivery pens. To vary the dosage amounts available to a user would require more complex devices that are costly to manufacture. Hence, it is necessary to provide a medication delivery pen at a reasonable cost having a wider range of doses and more flexibility when setting doses for drug delivery.

SUMMARY OF THE INVENTION

The subject invention relates to a medication delivery pen having a medication cartridge assembly that is selectively engageable with and disengageable from a

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pen body assembly. The medication cartridge assembly is an elongate generally cylindrical structure having opposed proximal and distal ends. The distal end of the medication cartridge assembly includes needle mounting means for securely but releasably receiving a needle cannula assembly, the distal end being characterized by a pierceable elastomeric seal that may be repeatedly and resealably pierced by the proximal end of a double-ended needle cannula. The proximal end of the medication cartridge assembly includes body mounting means for securely but releasably mounting the medication cartridge assembly to the pen body assembly. The body mounting means may comprise an array of threads extending distally from the proximal end of the medication cartridge assembly.

The medication cartridge assembly further includes plunger means slidably disposed in fluid tight engagement therein. The plunger means may initially be disposed in a proximal position within the medication cartridge assembly and may be moved in a distal direction by a driver projecting from the pen body assembly. The medication cartridge assembly further comprises anti-rotation means for preventing rotation of the driver.

The pen body assembly of the subject invention comprises an array of mounting threads to enable threaded engagement of the pen body assembly and the medication cartridge assembly and an actuator button rotatably mounted on its proximal end. Thus, axial forces exerted on the actuator button cause the pen body assembly to threadedly engage the medication cartridge assembly.

The pen body assembly further includes a lead screw for selectively engaging the plunger of the cartridge assembly and for urging the plunger of the cartridge assembly in a distal direction. At least a portion of the lead screw includes driving threads engaged with other portions of the pen body assembly that may be operative to achieve axial movement of the lead screw in response to axial forces exerted on the rotatable actuator button. The pen body assembly further comprises dose setting means for establishing and precisely controlling the amount of medication to be delivered in response to each actuation of the actuator button. The dose setting means may be any of several structures as described in greater detail below.

A cartridge assembly that is filled with medication is mounted to the pen body assembly and the initial response to forces on the actuator button cause the lead screw to move in a proximal direction toward its starting position, while the remaining portions of the pen body assembly move distally toward the vial assembly. Further forces exerted on the actuator button cause the mounting means of the pen body to engage the mounting means of the cartridge assembly. Continued axial forces on the actuator button cause the mounting threads to engage the cartridge assembly and continue the proximal movement of the driver. The pen body assembly is fully but releasably engaged with the cartridge assembly at

the same time that the driver is at its proximal extreme position and is then in position to begin delivering selected doses of medication from the pen. Doses of medication can be dispensed as needed over time, and the cartridge assembly is removed and discarded when the medication therein has been exhausted. A new medication cartridge assembly may then be mounted to the pen body assembly as described above.

The driving means in the pen body assembly of the present invention includes a dose setting knob having a helical groove with three different regions of operation, each region having a different pitch to provide three different types of dosage increments. For example, the dose setting increments in the first region are 0.5 within a dose range of 0 to 10 units, 1.0 in the 10 to 30 unit range of the second region, and 2.0 for doses above 30 units in the third region. This approach to dose setting and the associated resolution (ability to select a particular dose) is believed to be more consistent with the way insulin doses are prescribed by physicians and the way patients are instructed to adjust their own insulin dose.

#### DESCRIPTION OF THE DRAWINGS

Fig. 1 is a perspective view of the medication delivery pen of the subject invention.

Fig. 2 is an exploded perspective view of the pen body assembly of the medication delivery pen shown in Fig. 1.

Fig. 3 is a side view of the periphery of a dose knob of the present invention operating in a first region and projected on a plane.

Fig. 4 is a side view of the periphery of a dose knob of the present invention operating in a second region and projected on a plane.

Fig. 5 is a side view of the periphery of a dose knob of the present invention operating in a third region and projected on a plane.

#### DETAILED DESCRIPTION

A medication delivery pen in accordance with the subject invention is identified generally by the numeral 10 in Fig. 1. Medication delivery pen 10 includes a pen body assembly 12, a cartridge assembly 14, a needle cannula assembly 16 and a cap 17. Cartridge assembly 14 includes opposed proximal and distal ends 18 and 20, respectively. Proximal end 18 of cartridge assembly 14 is dimensioned and configured to threadedly engage pen body assembly 12, as explained further herein. Distal end 20 of cartridge assembly 14 is configured to securely but releasably engage needle cannula assembly 16 and a shield 130 is provided to cover a distal end 126 of a needle cannula 122 in needle cannula assembly 16.

The preferred embodiment of pen body assembly 12 is illustrated in greater detail in Fig. 2. It is understood, however, that variations from this preferred embodiment is provided, and are considered to be within the scope

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of the subject invention. Pen body assembly 12 includes a generally cylindrical housing 22 having opposed proximal and distal ends 24 and 26, and a substantially hollow throughbore 28 extending axially therethrough. An array of external threads 30 extends proximally from distal end 26 for threaded engagement with proximal end 16 of cartridge holder assembly 14. Portions of hollow throughbore 28 of housing 22 adjacent distal end 26 are characterized by an array of clutch teeth (not shown) molded therein. Proximal end 24 of housing 22 is characterized by a cut-out 33 formed therein for receiving a window insert 78.

Pen body assembly 12 includes a nut 34 having opposed proximal and distal ends 36 and 38, respectively. Exterior surface regions of nut 34 between proximal and distal ends 36 and 38 define a plurality of longitudinally extending splines 39. Proximal end 36 of nut 34 also includes a plurality of longitudinally extending resilient fingers 40 with enlarged ends that enable snap engagement of nut 34 into other portions of pen body assembly 12, as explained further herein. Distal end 38 of nut 34 is radially enlarged to limit axial movement of nut 34 in distal end 26 of housing 22. Thus, nut 34 is axially constrained within housing 22, however, the dimensions and configurations of nut 34 and housing 22 permit free relative rotation therebetween.

Pen body assembly 12 includes a clutch assembly 42 mounted therein. Clutch assembly 42 includes a proximal clutch 44, a distal clutch 46 and an annular spring 48 biasingly engaged therebetween. Proximal and distal clutches 44 and 46 each are configured for non-rotatable engagement over splines 39 of nut 34. Distal clutch 46 includes an array of distally facing saw teeth dimensioned, disposed and configured for engagement with clutch teeth (not shown) on the interior distal end of housing 22, such that distal clutch 46 can rotate only in one direction relative to housing 22. Proximal clutch 44 includes an array of proximally facing teeth which are also configured for unidirectional rotation, as explained further herein.

Pen body assembly 12 includes a generally cylindrical driver 50 having opposed proximal and distal ends 52 and 54. Driver 50 is slidably inserted into housing 22 of pen body assembly 12 such that distal end 54 of driver 50 is snap fit over the enlarged ends of resilient fingers 40 at proximal end 36 of nut 34. This snap fit engagement prevents axial movement between nut 34 and driver 50, but permits free relative rotational movement within housing 22. Distal end 54 of driver 50 is also characterized by an array of saw teeth 49 that engage with the saw teeth on proximal clutch 44. Outer surface regions of driver 50 are characterized by splines 56 extending radially outwardly thereon and along a substantial portion of the length of driver 50.

Pen body assembly 12 includes a dose knob 58 which is a hollow generally cylindrical structure having opposed proximal and distal ends 60 and 62 and opposed inner and outer surfaces 64 and 66. Inner surface

64 is characterized by longitudinally extending grooves 68 which are disposed and dimensioned for engagement with splines 56 on driver 50. More particularly, dose knob 58 is spline mounted over driver 50 within housing 22 of pen body assembly 12. Thus, axially extending grooves 68 in dose knob 58 engage splines 56 of driver 50 to prevent relative rotation therebetween, but permitting relative axial movement.

Figs. 3-5 are side views of the periphery of dose setting knob 58 projected on a plane and show button 86 operating in a first, second and third region, respectively. As shown in Figs. 3-5, outer surface 66 of dose knob 58 is characterized by a groove 70 comprised of three regions, each region having a helical component 174, 184, 194. Each helical component has a different pitch to provide different dose increments in each region of dose setting knob 58 and thereby improve resolution and provide a greater range of potential dosage settings for the pen. Outer surface 66 adjacent each helical component 174, 184, 194 of groove 70 is provided with dosage indicia to define dose setting increments corresponding to each region of groove 70. For example, the dose setting increments are 0.5 in the dose range 0 to 10 units of helical component 174, 1.0 in the 10 to 30 unit range of helical component 184, and 2.0 for doses above 30 units in helical component 194. The present invention provides dosage resolution very consistent with the way insulin doses are prescribed by physicians, and the way patients are instructed to adjust their own insulin dosages.

Proximal end 60 of dose knob 58 is characterized by a grained exterior surface to facilitate manipulation for setting a selected dose. An actuator button 76 is snapped into engagement with proximal end 60 of dose knob 58 to permit relative rotation therebetween. An insert 78 is snapped into engagement with cut-out 33 in proximal end 24 of housing 22, insert 78 including opposed inner and outer surfaces 82 and 80 and a window 84 extending therebetween. Inner surface 82 of insert 78 includes a button 86, shown in Figs. 3-5, on inner surface 82 dimensioned and disposed to engage in groove 70 of dose knob 58. Button 86 and window 84 are also disposed to enable the indicia on dose knob 58 to be visible through window 84.

Pen body assembly 12 further includes a lead screw 88 with opposed proximal and distal ends 90 and 92 and an array of external threads 94. External threads 94 are characterized, however, by a pair of opposed axially extending grooves 96 which extend from distal end 92 substantially to the proximal end 90. Threads 94 are engaged in nut 34, such that proximal end 90 of lead screw 88 is within housing 22 and distal end 92 projects distally beyond housing 22. Threads 94 on lead screw 88 have exactly the same pitch and the same hand as threads 30 on distal end 26 of housing 22.

Pen body assembly 12 is assembled by placing nut 34 into housing 22 from distal end 26. Clutch assembly 42 then is mounted over splines 39 on nut 34. Driver 50 is then inserted into proximal end 24 of housing 22, and

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is urged sufficiently in a distal direction for snap fit engagement with nut 34. In this snapped engagement, the saw teeth of distal clutch 46 will be secured in engagement with the teeth in housing 22, and the saw teeth of proximal clutch 44 will be engaged with saw teeth 49 at distal end 54 of driver 50. Spring 48 will maintain constant selected pressure between these interengaged saw teeth. Insert 78 then is positioned over dose knob 58 such that button 66 of insert 78 is engaged in groove 70 in dose knob 58. The temporarily assembled insert 78 and dose knob 58 then are urged into housing 22. Lead screw 88 then is threaded into nut 34, and actuator button 76 is snapped into engagement with proximal end 60 of dose knob 58.

The assembled pen body assembly 12 and cartridge assembly 14, shown in Fig. 1, is stored until a selected dose of medication is required. Just prior to use, needle cannula assembly 16 is threadably engaged to distal end 20 of cartridge assembly 14. This threaded engagement will cause a proximal tip 124 of needle cannula 122 to pierce a seal on the medication cartridge and provide communication with medication therein. Shield 130 may then be removed. A desired dose of medication is set by rotating dose knob 58 until indicia corresponding to the desired dose appears in window 84 of insert 76. The engagement of button 66 on insert 78 in helical portions 174, 184, 194 of groove 70 in dose knob 58 causes a threaded retraction of dose knob 58 relative to housing 22 of pen body assembly 12. This threaded retraction of dose knob 58 will cause a simultaneous rotation of driver 50 spined thereto. However, nut 34 will not rotate because the saw teeth on distal clutch 46 and the saw teeth on interior portions of housing 22 are locked to prevent rotation in that direction. Proximal clutch 44 is spined to nut 34, and hence also will not turn. However, saw teeth 49 at distal end 54 of driver 50 are shaped to allow rotation relative to proximal clutch 44, and provide an audible click for each unit of medication in the selected dose. This is helpful for visually impaired patients who may be required to set doses and administer insulin or other medication to themselves. Annular spring 48 contributes to the engagement that provides these audible clicking sounds.

When the desired dose is set, injection is achieved by merely pushing on actuator button 76. This causes dose knob 58 to turn about helices 174, 184, 194 relative to pen body housing 22, so that driver 50 rotates through the same number of degrees. As dose knob 58 turns about helices 174, 184, 194, button 66 travels through helix 174 in the first region when dispensing 1 to 10 units of medication, helix 184 in the second region when dispensing 11 to 30 units of medication, and helix 194 in the third region when dispensing 31 to 50 units of medication. Dose setting knob 58 of the present invention therefore provides a wider range of dosages for the user than previously known dose setting knobs because of the different pitch of each helix, as shown in Figs. 3-5. Rotation of dose setting knob 58 is opposite to the rotation gen-

erated during the dose setting procedure, when the rotational freedom of clutch assembly 42 is reversed. As dose setting knob 58 turns during injection the previously clicking proximal clutch 44 is locked to and turns with driver 50. This driving movement of proximal clutch 44 causes a corresponding rotational movement of nut 34 because of the spined engagement therebetween. Distal clutch 46 is therefore free to rotate against the saw teeth in housing 22, and makes an audible clicking indication during injection of medication.

Rotation of lead screw 88 is prevented by grooves 96 and tabs unitarily molded within housing 100 of cartridge holder assembly 14. Therefore, as nut 34 rotates under the driving action of proximal clutch 44 and driver 50, lead screw 88 will be advanced axially into cartridge holder assembly 14. This axial advancement of lead screw 88 causes distal end 92 thereof to urge plunger 116 distally into cartridge 106, and hence causes a particular amount of medication to be injected through needle cannula 122 depending upon the dosage set using dose setting knob 58. Injection is terminated when proximal end 68 of dose knob 58 engages against proximal end 24 of pen body housing 22.

Upon completion of the injection, needle cannula assembly 16 may be disengaged from cartridge holder assembly 14 and safely discarded. Cap 17 may be mounted over cartridge holder assembly 14, and pen 10 may be stored or carried in a convenient location until the next dose of medication is required. A subsequent dose of medication will be set in exactly the manner as described above. However, for such a subsequent dose, lead screw 88 will be in a partly advanced position as a starting point. Dose setting and injections can be carried out until all of the medication has been used. Cartridge holder assembly 14 may then be threadably disengaged from pen body assembly 12, and slidably separated from lead screw 88. The separated cartridge holder assembly may then be discarded and replaced as described above.

While the invention has been described with respect to a preferred embodiment, it is apparent that various changes can be made without departing from the scope of the invention as defined by the appended claims. In particular, the pen body assembly may have other driving and/or clutch mechanisms. Additionally, different means for preventing and/or enabling rotation during the dose setting and injection phases may be provided. Similarly, other means for mounting needle cannula to the cartridge assembly may be provided. These various optional constructions will be apparent to those skilled in the art after having read the subject disclosure.

#### Claims

1. A medication delivery pen comprising:
  - a medication-containing cartridge assembly having a pierceably sealed distal end, an open proximal end having an array of threads, and a plunger

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in sliding fluid tight engagement within said cartridge at a location distally of said array of threads; and a pen body assembly having:

a housing with opposed proximal and distal ends, said distal end having an array of threads dimensioned and pitched for threaded engagement with said threads at said proximal end of said cartridge;

a lead screw having a proximal end disposed in said housing, a distal end projecting beyond said distal end of said housing for selective engagement with said plunger, and threads extending between said proximal and distal ends of said lead screw; and

a dose setting knob having two or more regions of operation, each region having a plurality of dosage indicia for a predefined range of dosage increments, said dose setting knob being used to move said lead screw distally in said pen body assembly a distance corresponding to the selected region of operation and dosage indicia.

2. The medication delivery pen of Claim 1, wherein said pen body assembly further includes an actuator button rotatably mounted on said dose setting knob, such that axial forces exerted on said actuator button generate movement of said lead screw distally in said pen body assembly and into said cartridge.

3. The medication delivery pen of Claim 1, wherein said dose setting knob defines specified distances of travel for said lead screw corresponding to selected doses of medication to be delivered.

4. The medication delivery pen of Claim 1, wherein said seated end of said cartridge assembly comprises a pierceable elastomeric seal, and wherein said cartridge assembly further comprises needle mounting means adjacent said distal end of said cartridge assembly, said medication delivery pen further comprising a needle cannula assembly having a hub selectively engageable with the mounting means of said cartridge assembly and a double-ended needle having opposed proximal and distal points, said proximal point of said needle being dimensioned and disposed to pierce said seal upon engagement with said cartridge assembly.

5. The medication delivery pen of Claim 4, further comprising a plurality of needle cannula assemblies, each said needle cannula assembly being selectively engageable and disengageable from said cartridge assembly.

6. The medication delivery pen of Claim 1, wherein said lead screw of said pen body assembly includes a longitudinally extending groove therein, and wherein said cartridge assembly includes a tab for

slidably engaging the lead screw, whereby said tabs prevent relative rotation between said lead screw and said cartridge assembly.

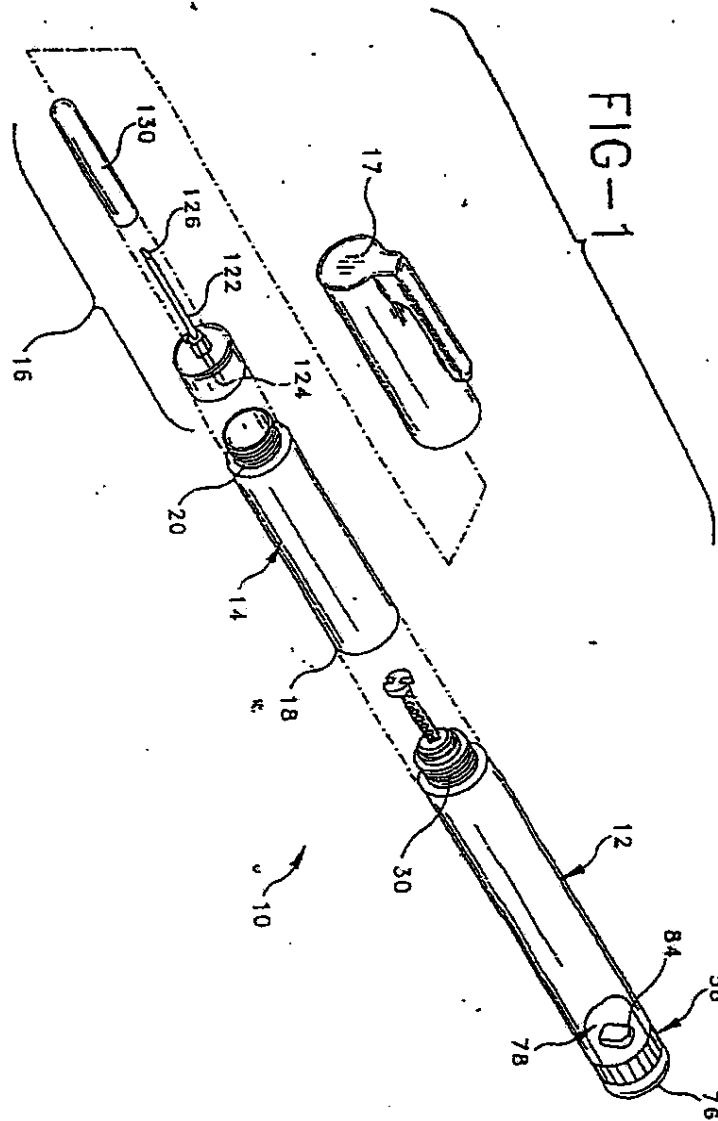
7. The medication delivery pen of Claim 1, wherein said pen body assembly includes a button and said dose setting knob includes a groove for receiving said button and thereby controlling movement of said lead screw distally in said pen body assembly and into said cartridge.

8. The medication delivery pen of Claim 7, wherein said groove on said dose setting knob has a different pitch in each region of said dose setting knob, wherein each pitch provides for different dosage increments.

9. The medication delivery pen of Claim 1, wherein said pen body assembly includes a driver selectively movable in proximal and distal directions in said pen body assembly housing, said driver connecting said dose setting knob to said lead screw.

10. The medication delivery pen of Claim 9, wherein said threads on said lead screw define a pitch substantially identical to said pitch of said threads on said distal end of said housing, said lead screw being axially movable in said housing in response to movement of said driver by said dose setting knob for selectively advancing said lead screw distances from said housing corresponding to selected doses of medication,

whereby the substantially identical pitches of said threads on said lead screw and on said housing enables said lead screw to move in said housing simultaneously with threaded engagement of said housing with said cartridge holder assembly.

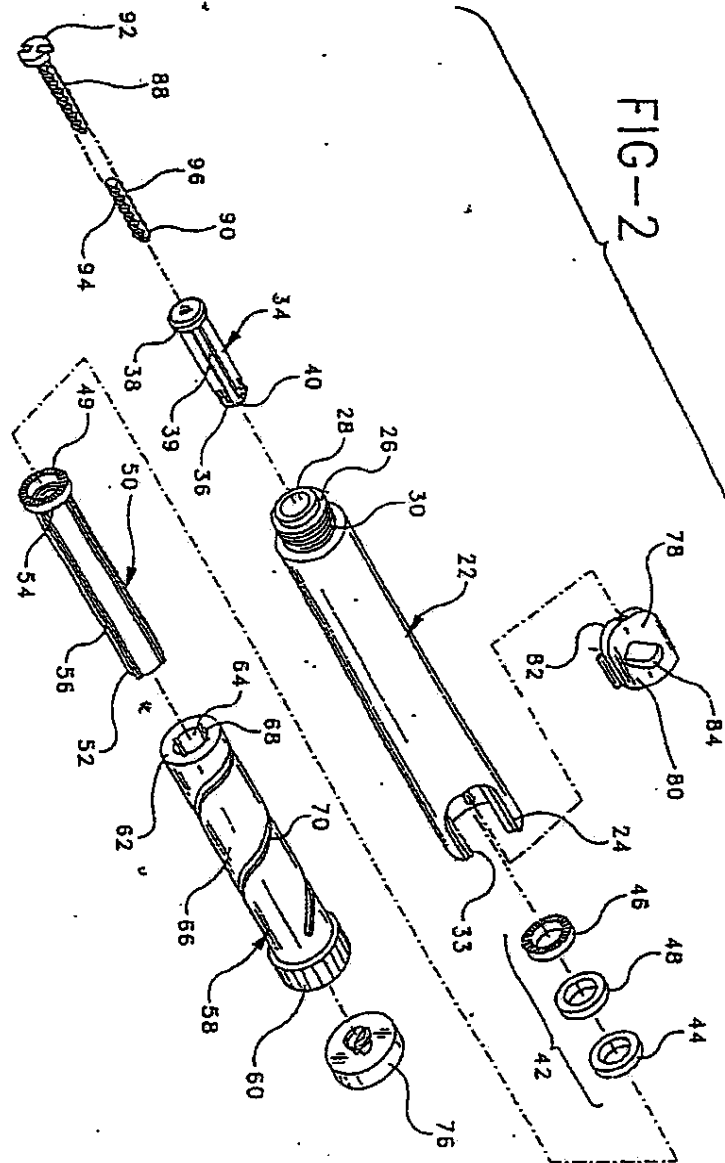


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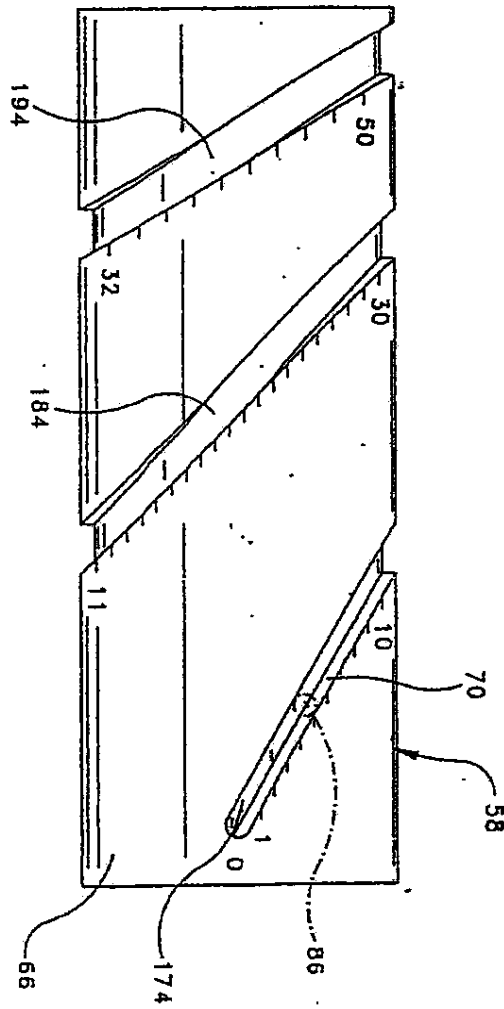
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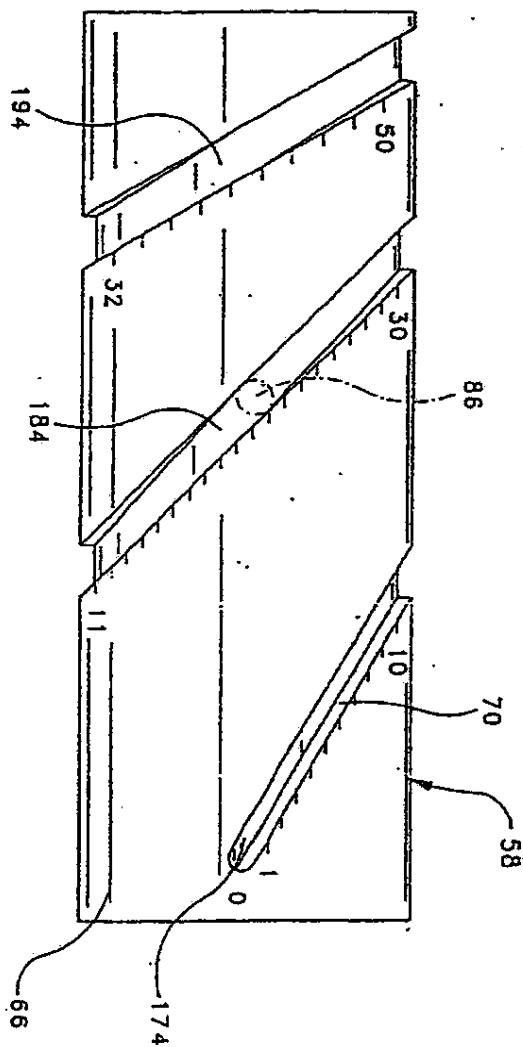
FIG-3



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FIG-4

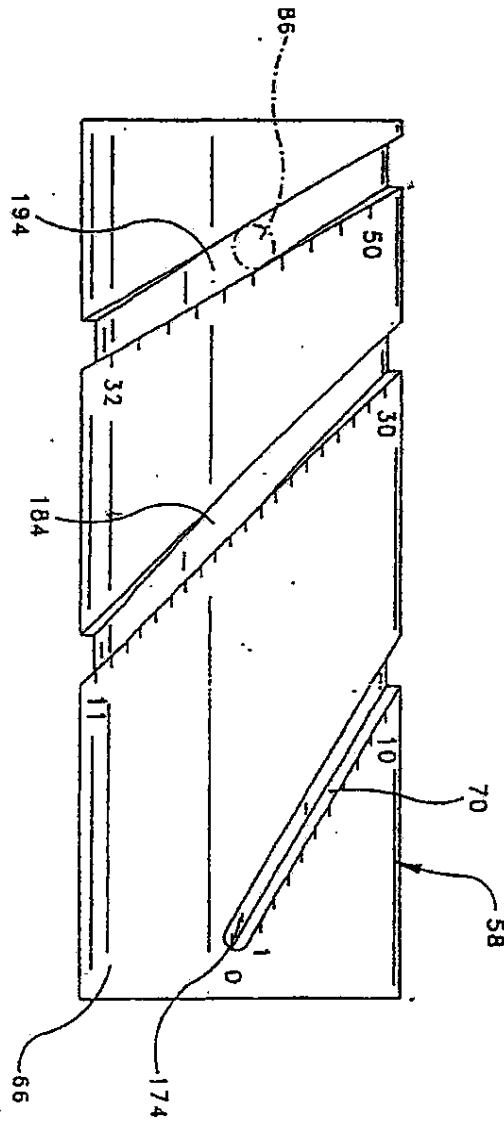


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FIG-5



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(54) Title: SYRINGE SYSTEM		
<p>(57) Abstract</p> <p>An insulin injection system comprises a pen shaped syringe with a cartridge containing insulin, and an injection needle. The needle is a G 30 needle and the insulin is a type which may freely flow through a G 30 needle. When the insulin is the type comprising suspended crystals the maximal dimension of any crystal is 15 µm.</p>		

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## SYRINGE SYSTEM

The invention relates to syringes for injecting insulin and more specified pen-shaped syringes administering insulin doses from a cartridge in the pen syringe.

5 Diabetes is usually treated by the patient frequently injecting himself with an insulin dose which he adjusts each time according to his immediate need.

To make it less straining to the patient to prick himself several times a day, it is aspired to make the injections as painless as possible and to reduce the psychical malaise many people will feel if they have to pass a needle into their  
10 own body.

As the malaise seems to grow with the length and the thickness of the needle and the sensation of pain seems to be reduced when the needle is made thinner, a passable way seems to be to make the needle thinner and shorter. This line may, of course, only be followed to a certain extent, as the  
15 needle must have a length permitting the subcutaneous injection of the insulin and a thickness allowing the insulin to pass through the needle.

Whereas the acceptable minimum length of the needle is well defined, the lower limit for the thickness of the needle is more fluid. With a thinner needle it becomes more difficult to press the insulin out through the needle and  
20 the injections will take more time. A more relevant lower limit is set by the fact that by injecting insulin types appearing as suspended crystals, a sieving of the suspension may occur, and the suspension injected may consequently have a lower concentration than expected.

The thicknesses of needles are indicated by a "G" and a gauge  
25 number, increasing with thinner needles. Thus, the outer diameter of a G 27 needle is 0.4 mm, of a G 28 needle 0.36 mm, and of a G 30 needle 0.3 mm. The wall thickness of the needles is typically 0.075 mm, so that a G 27 needle has a bore of 0.25 mm, whereas the bore of a G 30 needle is 0.15 mm.

Commonly, G 27 needles are used. However, according to Diabetes  
30 Forecast 1976; 29 page 27 problems are observed when G 27 needles and even thicker needles are used for injecting an insulin containing suspended crystals.

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The problem is a clogging of the needle during injection, which clogging is due to the fact that crystals of e.g. Lente insulin having a size of 20 - 40  $\mu\text{m}$  have a tendency to align themselves across the inside of the needle. This clogging is observed during injection, especially if this injection is carried out too slowly. It must be presumed that a similar clogging occurs during the filling of the syringe thus making the filling impossible or at least having the effect that some of the crystals are retained with the consequence that the suspension sucked into the syringe has a lower concentration than expected.

Whereas the trend goes towards the use of G 28 needles this is seen as close to the limit of what is possible. G 29 needles are seen as needles for disposable syringes for insulin, but G 30 needles have so far been deemed unusable for injection of an insulin suspension.

The present invention is based on the surprising recognition that needles thinner than G 29 may be used for injecting insulin.

The present invention is, thus, related to an insulin injection system comprising a pen shaped syringe having a cartridge with insulin and an injection needle, the system being characterized in that the needle is a G 30 needle and the cartridge contains an insulin type which may flow freely through a G 30 needle.

By the use of a pen shaped syringe with a cartridge the insulin will only have to pass the needle once, which in itself halves the risk of sieving. Further, the use of suspensions of insulin types having very short and needle shaped crystals totally eliminates the risk of bridging in a G 30 needle when no dimension of the insulin crystals exceeds 15  $\mu\text{m}$ .

By closely binding a G 30 needle to a system further comprising a pen-shaped syringe, it may be ensured that a pen syringe equipped with a G 30 needle will always contain insulin of a type which may pass through the needle without any sieving effect.

The pen syringe may either be manufactured as a disposable device which is sold prefilled with the insulin or it may appear as a durable pen syringe so designed that it can only receive cartridges with insulin which may pass freely through a G 30 needle.

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The needle may have attaching means cooperating with attaching means on the pen syringe for mounting the needle on the pen syringe, whereby the needle hub may be designed to only match with pen syringes of the system. Such attaching means may be a needle hub having a thread cooperating with a  
5 corresponding thread on the syringe.

The needle hub may have a central protrusion covering part of the length of the needle. Thereby, the length of the injection part of the needle is made shorter, which is advantageous as well from a psychological point of view as from a mechanical one. The protrusion makes visible only the part which  
10 should be inserted and it supports the thin and consequently more fragile needle.

With an injection part of the needle of 8 - 12 mm, it is avoided that the injections become intermuscular instead of subcutaneous. The needles may be manufactured in the same length as usual for thicker needles and the shorter injection part may be obtained by the hub protrusion covering a larger part than  
15 usual for the needle.

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## CLAIMS

1. An insulin injection system comprising a pen shaped syringe comprising a cartridge with insulin and an injection needle, characterized in that the needle is a G 30 needle and the cartridge contains an insulin type which may freely flow through a G 30 needle.

2. An insulin injection system according to claim 1, characterized in that the insulin in the cartridge has a maximal crystals size of 15  $\mu\text{m}$ .

3. An insulin injection system according to claim 1 or 2, characterized in that the pen syringe is a disposable device prefilled with insulin.

10 4. An insulin injection system according to claim 1 or 2, characterized in that the pen syringe is a durable device designed to receive only cartridges containing insulin which may pass freely through a G 30 needle.

5. An insulin injection system according to any of the preceding claims, characterized in that the needle has attaching means for cooperation with  
15 attaching means on the pen syringe.

6. An insulin injection system according to claim 5, characterized in that the needle attaching means is a needle hub having a thread cooperating with a corresponding thread on the pen syringe.

7. An insulin injection system according to claim 6, characterized in  
20 that the needle hub has a central protrusion covering part of the length of the needle.

8. An insulin injection system according to claim 7, characterized in

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that the length of the injection part of the needle is 8 - 12 mm.

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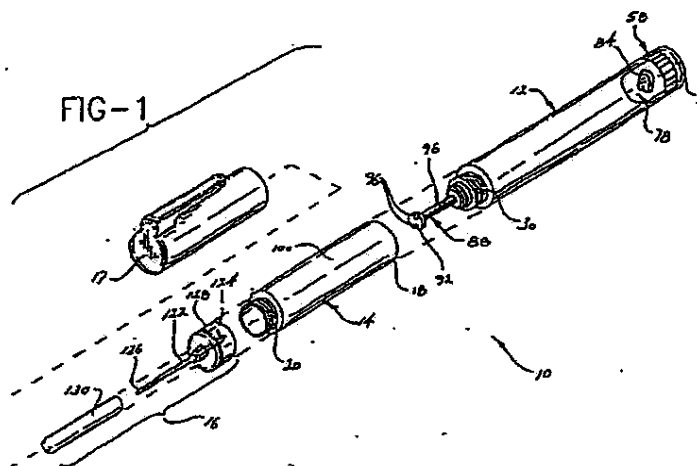
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(30) Quick connect medication delivery pen

(31) A medication delivery pen is provided having a reusable pen body assembly and a disposable cartridge assembly that are threadably engageable with one another. The disposable cartridge assembly includes a plunger and can releasably receive a needle cannula assembly. A portion of the pen body assembly projects into the cartridge holder assembly

for driving the cartridge plunger distances that are selected in accordance with a desired dose of medication to be delivered. The cartridge holder assembly can be disassembled from the pen body assembly after the medication therein has been exhausted, and the used cartridge holder assembly may be discarded and replaced.



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BACKGROUND OF THE INVENTION1. Field of the Invention

The subject invention relates to medication delivery pens having a disposable cartridge holder assembly and a reusable pen body assembly removably mounted to the cartridge holder assembly for delivering selected doses of medication.

2. Description of Related Art

Hypodermic syringes are used to deliver selected doses of medication to patients. The prior art hypodermic syringe includes a syringe barrel having opposed proximal and distal ends. A cylindrical chamber wall extends between the ends and defines a fluid receiving chamber. The proximal end of the prior art syringe barrel is substantially open and receives a plunger in sliding fluid tight engagement. The distal end of the prior art syringe barrel includes a passage communicating with the chamber. A needle cannula may be mounted to the distal end of the prior art syringe barrel, such that the lumen of the needle cannula communicates with the passage and the chamber of the syringe barrel. Movement of the plunger in a proximal direction draws fluid through the lumen of the needle cannula and into the chamber. Movement of the plunger in a proximal-to-distal direction urges fluid from the chamber and through the lumen of the needle cannula.

Medication to be injected with the prior art hypodermic syringe often is stored in a vial having a pierceable elastomeric seal. Medication in the prior art vial is accessed by piercing the elastomeric seal with the needle cannula. A selected dose of the medication may be drawn into the chamber of the syringe barrel by moving the plunger a selected distance in a proximal direction. The needle cannula may be withdrawn from the vial, and the medication may be injected into a patient by moving the plunger in a distal direction.

Some medication, such as insulin is self-administered. The typical diabetes patient will require injections of insulin several times during the course of the day. The required dose of insulin will vary from patient to patient, and for each patient may vary during the course of the day and from day to day. Each diabetes patient will establish a regimen that is appropriate for his or her own medical condition and for his or her lifestyle. The regimen typically includes some combination of a slow or medium acting insulin and a faster acting insulin. Each of these regimens may require the diabetes patient to periodically self-administer insulin in public locations, such as places of employment or restaurants. The required manipulation of the stan-

dard prior art hypodermic syringe and vial can be inconvenient and embarrassing in these public environments.

Medication delivery pens have been developed to facilitate the self-administration of medication. One prior art medication delivery pen includes a vial holder into which a vial of insulin or other medication may be received. The vial holder is an elongate generally tubular structure with proximal and distal ends. The distal end of the prior art vial holder includes mounting means for engaging a double-ended needle cannula. The proximal end also includes mounting means for engaging a driver and dose setting apparatus as explained further below. A disposable vial for use with the prior art vial holder includes a distal end having a pierceable elastomeric seal that can be pierced by one end of a double-ended needle cannula. The proximal end of this prior art vial includes a plunger slidably disposed in fluid tight engagement with the cylindrical wall of the vial. This prior art medication delivery pen is used by inserting the vial of medication into the vial holder. A prior art pen body then is connected to the proximal end of the vial holder. The pen body includes a dose setting apparatus for designating a dose of medication to be delivered by the pen and a driving apparatus for urging the plunger of the vial distally for a distance corresponding to the selected dose.

The user of the pen mounts a prior art double-ended needle cannula to the distal end of the vial holder such that the proximal point of the needle cannula pierces the elastomeric seal on the vial. The patient then selects a dose and operates the pen to urge the plunger distally to deliver the selected dose. The dose selecting apparatus returns to zero upon injection of the selected dose with this prior art medication delivery pen. The patient then removes and discards the needle cannula, and keeps the prior art medication delivery pen in a convenient location for the next required medication administration. The medication in the vial will become exhausted after several such administrations of medication. The patient then separates the vial holder from the pen body. The empty vial may then be removed and discarded. A new vial can be inserted into the vial holder, and the vial holder and pen body can be reassembled and used as explained above.

The above described reusable medication delivery pen is effective and much more convenient for self-administration of medication than the typical hypodermic syringe and separate medication vial. However, the disassembly of the pen to remove empty medication vials and to insert new ones is an inconvenience. As a result, disposable pens have been developed. The prior art disposable medication delivery pen includes a vial of

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insulin or other such medication permanently encapsulated therein. The patient need merely connect a double-ended needle cannula to the disposable pen for each administration of medication. The prior art disposable pen can be discarded when the supply of medication permanently encapsulated therein has been exhausted.

Disposable medication delivery pens offer certain conveniences to the patient who is required to self-administer medication. However, the dose selecting and driving mechanisms of prior art medication delivery pens are fairly complex devices that are costly to manufacture. Hence, a substantial cost penalty is associated with the convenience of using a disposable medication delivery pen.

#### SUMMARY OF THE INVENTION

The subject invention relates to a medication delivery pen having a disposable medication cartridge assembly that is selectively engageable with and disengageable from a reusable pen body assembly. The disposable medication cartridge assembly is an elongate generally cylindrical structure having opposed proximal and distal ends. The distal end of the disposable medication cartridge assembly includes needle mounting means for securely but releasably receiving a needle cannula assembly. The distal end may be characterized by a pierceable elastomeric seal that may be repeatedly and resealably pierced by the proximal end of a double-ended needle cannula. The proximal end of the disposable medication cartridge assembly includes body mounting means for securely but releasably mounting the disposable medication cartridge assembly to the reusable pen body assembly. The body mounting means may comprise an array of threads extending distally from the proximal end of the disposable medication cartridge assembly.

The disposable medication cartridge assembly further includes plunger means slidably disposed in fluid tight engagement therein. The plunger means may initially be disposed in a proximal position within the medication cartridge assembly and may be moved in a distal direction by a driver projecting from the pen body assembly. The disposable medication cartridge assembly further comprise anti-rotation means for preventing rotation of the driver.

The reusable pen body assembly of the subject invention comprises an array of mounting threads to enable threaded engagement of the reusable pen body assembly and the disposable medication cartridge assembly. An actuator button may be rotatably mounted on the proximal end of the pen body assembly. Thus, axial forces exerted on the actuator button will cause the pen body

assembly to threadedly engage the disposable medication cartridge assembly.

The pen body assembly further includes a lead screw for selectively engaging the plunger of the disposable cartridge assembly and for urging the plunger of the disposable cartridge assembly in a distal direction. At least a portion of the lead screw may have driving threads engaged with other portions of the pen body assembly. This threaded engagement may be operative to achieve axial movement of the lead screw in response to axial forces exerted on the rotatable actuator button. The driving threads may define the same pitch and the same direction of generation as the mounting threads of the pen body assembly. As will be explained in greater detail below, this feature of the medication delivery pen facilitates the quick connection of the pen body assembly to the disposable medication cartridge assembly, and further assures a virtually automatic return of the lead screw to a start position each time a new disposable medication cartridge assembly is mounted to the pen body assembly. The lead screw may further be engageable with the anti-rotation means of the disposable cartridge assembly. Thus, relative rotation between the lead screw means and the disposable cartridge assembly is substantially prevented.

The pen body assembly further comprises a dose setting means for establishing and precisely controlling the amount of medication to be delivered in response to each actuation of the actuator button. The dose setting means may be any of several structures as described in greater detail below.

A disposable cartridge assembly that is filled with medication may be mounted to the pen body assembly by merely aligning the lead screw with the proximal end of the disposable cartridge assembly and exerting an axial force on the rotatable actuator button. The initial response to forces on the actuator button will cause the lead screw to move in a proximal direction toward its starting position, while the remaining portions of the pen body assembly move distally toward the disposable vial assembly. Further forces exerted on the actuator button will cause the mounting means of the pen body to engage the mounting means of the disposable cartridge assembly. Continued axial forces on the actuator will cause the mounting threads to engage the disposable cartridge assembly and will continue the proximal movement of the driver. The pen body assembly will be fully but releasably engaged with the disposable cartridge assembly at the same time that the driver is at its proximal extreme position and in condition to begin delivering selected doses of medication from the pen. Doses of medication can be dispensed as

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needed over time. The disposable cartridge assembly can be removed and discarded when the medication therein has been exhausted, and a new disposable medication cartridge assembly may be mounted to the pen body assembly as described above.

#### DESCRIPTION OF THE DRAWINGS

Fig. 1 is an exploded perspective view of the medication delivery pen of the subject invention.

Fig. 2 is an exploded perspective view of the pen body assembly of the medication delivery pen shown in Fig. 1.

Fig. 3 is an end view of the housing of the pen body assembly.

Fig. 4 is a cross-sectional view of the nut taken along line 4-4 in Fig. 2.

Fig. 5 is a cross-sectional view of the insert taken along line 5-5 in Fig. 2.

Fig. 6 is an end elevational view of the cartridge holder assembly.

Fig. 7 is a longitudinal cross-sectional view of the pen in a first partly assembled condition.

Fig. 8 is a cross-sectional view similar to Fig. 7, and showing the pen in a second partly assembled condition.

Fig. 9 is a cross-sectional view similar to Figs. 7 and 8, and showing the pen in a fully assembled condition.

Fig. 10 is a cross-sectional view similar to Fig. 9, and showing the assembled pen in condition to deliver a selected dose of medication.

Fig. 11 is a cross-sectional view similar to Fig. 10 and showing the pen after delivery of the selected dose.

#### DETAILED DESCRIPTION

A medication delivery pen in accordance with the subject invention is identified generally by the numeral 10 in Figs. 1 and 7-11. Medication delivery pen 10 includes a reusable pen body assembly 12, a disposable cartridge assembly 14, a needle cannula assembly 16 and a cap 17. Cartridge assembly 14 includes opposed proximal and distal ends 18 and 20 respectively. Proximal end 18 of cartridge assembly 14 is dimensioned and configured to threadedly engage pen body assembly 12, as explained further herein. Distal end 20 of cartridge assembly 14 is configured to securely but releasably engage needle cannula assembly 16.

The preferred embodiment of reusable pen body assembly 12 is illustrated in greater detail in Fig. 2. It is understood, however, that variations from this preferred embodiment may be provided, and are considered to be within the scope of the subject invention. Reusable pen body assembly 12

includes a generally cylindrical housing 22 having opposed proximal and distal ends 24 and 26, and a substantially hollow throughbore 28 extending axially therethrough. An array of external threads 30 extends proximally from distal end 26 for threaded engagement with proximal end 18 of cartridge holder assembly 14. Portions of hollow throughbore 28 of housing 22 adjacent distal end 26 are characterized by an array of clutch teeth 32, shown in Fig. 3, molded therein. Proximal end 24 of housing 22 is characterized by a cut-out 33 formed therein for receiving a window insert 78, as shown in Fig. 5 and explained further herein.

Pen body assembly 12 further includes a nut 34 having opposed proximal and distal ends 36 and 38 respectively. Exterior surface regions of nut 34 between proximal and distal ends 36 and 38, shown in Fig. 4, define a plurality of longitudinally extending splines 39. Proximal end 36 of nut 34 is characterized by a plurality of longitudinally extending resilient fingers 40 with enlarged ends that enable snap engagement of nut 34 into other portions of pen body assembly 12 as explained further herein. Distal end 38 of nut 34 is radially enlarged to limit axial movement of nut 34 into distal end 26 of housing 22. Thus, nut 34 is axially constrained within housing 22. However, the dimensions and configurations of nut 34 and housing 22 permit free relative rotation therebetween.

Pen body assembly 12 further includes a clutch assembly 42 mounted therein. Clutch assembly 42 includes a proximal clutch 44, a distal clutch 46 and an annular spring 48 biasingly engaged therebetween. Proximal and distal clutches 44 and 46 each are configured for non-rotatable engagement over splines 39 of nut 34. Distal clutch 46 includes an array of distally facing saw teeth dimensioned, disposed and configured for engagement with teeth 32, shown in Fig. 3, on the interior of housing 22, such that distal clutch 46 can rotate only in one direction relative to housing 22. Proximal clutch 44 includes an array of proximally facing teeth which are also configured for unidirectional rotation as explained further herein.

Pen body assembly 12 further includes a generally cylindrical driver 50 having opposed proximal and distal ends 52 and 54. Driver 50 is slidably inserted into housing 22 of pen body assembly 12 such that distal end 54 of driver 50 is snap fit over the enlarged ends of resilient fingers 40 at proximal end 36 of nut 34. This snap fit engagement prevents axial movement between nut 34 and driver 50, but permits free relative rotational movement within housing 22. Distal end 54 of driver 50 is also characterized by an array of saw teeth 49 that engage with the saw teeth on proximal clutch 44. Outer surface regions of driver 50 are characterized by splines 56 extending radially outwardly



thereon and along a substantial portion of the length of driver 50.

Pen body assembly 12 further includes a dose knob 58 which is a hollow generally cylindrical structure having opposed proximal and distal ends 60 and 62 and opposed inner and outer surfaces 64 and 66. Inner surface 64 is characterized by longitudinally extending grooves 68 which are disposed and dimensioned for engagement with splines 56 on driver 50. More particularly, dose knob 58 is spline mounted over driver 50 within housing 22 of pen body assembly 12. Thus, axially extending grooves 68 in dose knob 58 engage splines 56 of driver 50 to prevent relative rotation therebetween, but permitting relative axial movement. Outer surface 66 of dose knob 58 is characterized by a groove 70 that includes a linear component 72 and a helical component 74, which connects opposed ends of linear component 72. Portions of outer surface 66 adjacent helical component 74 of groove 70 are provided with dosage indicia to define dose amounts corresponding to different positions along groove 70 as explained further herein. Proximal end 60 of dose knob 58 is characterized by a gnarled exterior surface to facilitate manipulation for setting a selected dose. An actuator button 76 is snapped in to engagement with proximal end 60 of dose knob 58 to permit relative rotation therebetween.

An insert 78, shown in Figs. 2 and 5, is snapped into engagement with cut-out 33 in the proximal end 24 of housing 22. Insert 78 includes opposed inner and outer surfaces 80 and 82 and a window 84 extending therebetween. Inner surface 80 of insert 78 includes a button 86 on an interior face which is dimensioned and disposed to engage in groove 70 of dose knob 58. Button 86 and window 84 are disposed to enable the indicia on dose knob 58 to be visible through window 84.

Pen body assembly 12 further includes a lead screw 88 with opposed proximal and distal ends 90 and 92 and an array of external threads 94. External threads 94 are characterized, however, by a pair of opposed axially extending grooves 96 which extend from distal end 92 substantially to the proximal end 90. Threads 94 are engaged in nut 34, such that proximal end 90 of lead screw 88 is within housing 22 and distal end 92 projects distally beyond housing 22. Threads 94 on lead screw 88 have exactly the same pitch and the same hand as threads 30 on distal end 26 of housing 22.

Pen body assembly 12 is assembled by placing nut 34 into housing 22 from distal end 26. Clutch assembly 42 then is mounted over splines 39 on nut 34. Driver 50 is then inserted into proximal end 24 of housing 22, and is urged sufficiently in a distal direction for snap fit engagement with nut 34. In this snapped engagement, the saw teeth

of distal clutch 46 will be secured in engagement with teeth 32 of housing 22, and the saw teeth of proximal clutch 44 will be engaged with saw teeth 49 at distal end 54 of driver 50. Spring 48 will maintain constant selected pressure between these interengaged saw teeth. Insert 78 then is positioned over dose knob 58 such that button 86 of insert 78 is engaged in the axial return track 72 of groove 70 in dose knob 58. The temporarily assembled insert 78 and dose knob 58 then are urged into housing 22. Lead screw 88 then is threaded into nut 34, and actuator button 76 is snapped into engagement with proximal end 60 of dose knob 58.

Cartridge assembly 14, shown in Figs. 1 and 6-11, includes a molded housing 100 which extends from proximal end 18 to distal end 20 of cartridge assembly 14, as noted above. Housing 100 includes a mounting cavity 102 extending inwardly from proximal end 18. Mounting cavity 102 is characterized by an array of internal threads 104 for threaded engagement with external threads 30 on distal end 26 of housing 22. The distal end of mounting cavity 102 is defined by anti-rotation tabs 106 which are dimensioned to slidably engage in slots 96 of lead screw 88. Thus, lead screw 88 can slidably move relative to anti-rotation tabs 106, but is prevented from rotating relative to tabs 106.

Cartridge holder assembly 14, as shown in Figs. 7-11, further includes a medication cartridge 108 securely retained in housing 100 between tabs 106 and distal end 20 of cartridge assembly 14. Medication cartridge 108 includes an open proximal end 110 and a distal end 112 having a pierceable elastomeric seal 114 securely mounted thereto. A cap 116 extends between housing 100 and cartridge 108 for securely and permanently holding medication cartridge 108 in housing 100. A plunger 118 is disposed in sliding fluid tight engagement in cartridge 108. As shown in Figs. 7-11, plunger 118 initially is disposed substantially adjacent proximal end 110 of medication cartridge 108. Portions of cartridge 108 between plunger 118 and seal 114 are filled with a medication 120, such as insulin.

Needle cannula assembly 16 includes a double ended needle cannula 122 having opposed proximal and distal points 124 and 126, respectively, and a lumen extending axially therebetween. A mounting hub 128 is engaged on needle cannula 122 and is removably engageable with cap 116 of cartridge holder assembly 14. The relative location of mounting hub 128 ensures that proximal point 124 of needle cannula 122 will pierce seal 114 when mounting hub 128 is engaged with cap 116. Needle cannula assembly 16 further includes a shield 130 removably mounted thereon for protecting against accidental needle sticks until immediately prior to use of pen 10.



As noted above, pen body assembly 12 is reusable, and cartridge holder assembly 14 is disposable. More particularly, cartridge 108 in cartridge holder assembly 14 will contain a volume of medication 120 sufficient for administration of several doses. After exhaustion of the medication 120, cartridge holder assembly 14 will be threadedly disengaged from pen body assembly 12 and discarded. A new cartridge holder assembly 14 may then be mounted to the reusable pen body assembly 12. To effect the mounting of a new cartridge holder assembly 14 to the reusable pen body assembly 12, the patient need merely align slots 96 at distal end 92 of lead screw 88 with tabs 106 at proximal end 18 of cartridge holder assembly 14. Distal end 92 of lead screw 88 is then advanced distally into cartridge holder assembly 14 until distal end 92 of lead screw 88 engages plunger 118, as shown in Fig. 7. Assembly continues by merely exerting axial forces on thumb swivel 76 and on cartridge holder assembly 14. Additionally, friction between plunger 118 and cartridge 108 and fluid forces exerted by medication 120 and seal 114 will prevent axial advancement of lead screw 88 beyond the position depicted in Fig. 9 during assembly. Additionally, the splined engagement of distal clutch 46 with nut 34 and the engagement of the teeth on distal clutch 46 with the corresponding teeth 32 on housing 22 prevents independent rotation of nut 34 during this initial mounting of reusable pen body assembly 12 with a new disposable cartridge assembly 14. Thus, axial forces exerted on thumb swivel 76 will cause cartridge housing 100 to threadedly advance along threads 94 of lead screw 88.

After sufficient axial advancement, threads 30 at distal end 26 of pen body housing 22 will engage internal threads 104 at proximal end 18 of cartridge holder assembly 14, as shown in Fig. 8. As noted above, external threads 30 at distal end 26 of housing 22 have exactly the same pitch and hand as threads 94 on lead screw 88. Hence, further axial forces exerted on thumb swivel 76 will cause the simultaneous threaded advancement of housing 22 along lead screw 88 and into cavity 102 at proximal end 18 of cartridge holder assembly 14. Thus, because of their identical pitches, lead screw 88 will move proximally relative to pen body housing 22, while pen body housing 22 and cartridge holder assembly 14 are approaching their fully seated and threaded condition depicted in Fig. 9.

The assembled reusable pen body assembly 12 and cartridge assembly 14 may be stored until a selected dose of medication is required. Just prior to use, a needle cannula assembly 16 may be threadedly engaged to distal end 20 of cartridge assembly 14. This threaded engagement will cause

proximal tip 124 of needle cannula 122 to pierce seal 114 and provide communication with medication 120. Shield 130 may then be removed.

A desired dose of medication 120 may be set by rotating dose knob 58 until indicia corresponding to the desired dose appears in window 84 of insert 78. The engagement of button 66 on insert 78 in helical portion 74 of groove 70 in dose knob 58 will cause a threaded retraction of dose knob 58 relative to housing 22 of reusable pen body assembly 12. This threaded retraction of dose knob 58 will cause a simultaneous rotation of driver 50 splined thereto. However, nut 34 will not rotate because the saw teeth on distal clutch 46 and saw teeth 32 on interior portions of housing 22 are locked to prevent rotation in that direction. Proximal clutch 44 is splined to nut 34, and hence also will not turn. However, saw teeth 49 at distal end 54 of driver 50 are shaped to allow rotation relative to proximal clutch 44, but provide an audible click for each unit of medication in the selected dose. This is helpful for visually impaired patients who may be required to set doses and administer insulin or other medication to themselves. Annular spring 48 contributes to the engagement that provides these audible clicking sounds.

When the desired dose is set, as shown in Fig. 10, injection is achieved by merely pushing on actuator button 76. This causes dose knob 58 to turn about helix 74 relative to pen body housing 22, and driver 50 rotates through the same number of degrees. This rotation is opposite to the rotation generated by the dose setting procedure, and the rotational freedom of the clutch assembly 42 is reversed. Thus, as driver 50 turns the previously clicking proximal clutch 44 is locked to and turns with driver 50. This driving movement of proximal clutch 44 causes a corresponding rotational movement of nut 34 because of the splined engagement therebetween. Distal clutch 46 is now free to rotate against saw teeth 32 on housing 22, and makes an audible clicking indication during injection of medication.

Rotation of lead screw 88 is prevented by tabs 106 unitarily molded with housing 100 of cartridge holder assembly 14. Therefore, as nut 34 rotates under the driving action of proximal clutch 44 and driver 50, lead screw 88 will be advanced axially into cartridge holder assembly 14. This axial advancement of lead screw 88 causes distal end 92 thereof to urge plunger 118 distally into cartridge 108, and hence causes medication 120 to be injected through needle cannula 122. Injection will be terminated when proximal end 60 of dose knob 58 engages against proximal end 24 of pen body housing 22, as shown in Fig. 11.

Upon completion of the injection, needle cannula assembly 16 may be disengaged from car-

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bridge holder assembly 14 and safely discarded. Cap 17 may be mounted over cartridge holder assembly 14, and pen 10 may be stored or carried in a convenient location until the next dose of medication is required. A subsequent dose of medication will be set in exactly the manner as described above. However, for such a subsequent dose, lead screw 88 and plunger 118 will be in a partly advanced position as a starting point. Dose setting and injections can be carried out until all of medication 120 has been used. Cartridge holder assembly 14 may then be threadably disengaged from pen body assembly 12, and slidably separated from lead screw 88. The separated cartridge holder assembly may then be discarded and replaced as described above.

While the invention has been described with respect to a preferred embodiment, it is apparent that various changes can be made without departing from the scope of the invention as defined by the appended claims. In particular, the reusable pen body assembly may have other driving and/or clutch mechanisms. Additionally, different means for preventing and/or enabling rotation during the dose setting and injection phases may be provided. Similarly, other means for mounting needle cannula to the cartridge assembly may be provided. These various optional constructions will be apparent to those skilled in the art after having read the subject disclosure.

#### Claims

1. A medication delivery pen comprising:
  - a disposable medication-containing cartridge having a pierceably sealed distal end and an open proximal end having an array of threads, a plunger in sliding fluid tight engagement within said cartridge at a location distally of said array of threads;
  - a reusable pen body assembly having a housing with opposed proximal and distal ends, said distal end having an array of threads dimensioned and pitched for threaded engagement with said threads at said proximal end of said cartridge, a lead screw having a proximal end disposed in said housing, a distal end projecting beyond said distal end of said housing for selective engagement with said plunger, and threads extending between said proximal and distal ends of said lead screw and defining a pitch substantially equal to said pitch of said threads at said distal end of said pen body assembly, said pen body assembly further comprising driver means for moving said lead screw distally in said pen body assembly selected amounts, whereby said lead screw is movable in a proximal direction in

said pen body assembly as said pen body assembly is threadably moved in a distal direction into engagement with said cartridge.

2. The medication delivery pen of Claim 1, wherein said pen body assembly further includes an actuator button rotatably mounted on said driver means, such that axial forces exerted on said actuator button simultaneously generate movement of said lead screw in a proximal direction in said pen body assembly and threaded engagement of said pen body assembly distally into said cartridge.
3. The medication delivery pen of Claim 1, wherein said lead screw includes at least one anti-rotation groove extending axially therealong, said cartridge including tab means for slidably engaging in said anti-rotation groove of said lead screw for preventing relative rotation between said lead screw and said cartridge.
4. The medication delivery pen of Claim 3, wherein said cartridge includes a housing unitarily molded from a plastic material, said tab being a unitary portion of said housing.
5. The medication delivery pen of Claim 1, wherein said cartridge defines a mounting cavity adjacent said proximal end thereof, said threads of said cartridge defining internal threads in said mounting cavity, said distal end of said pen body assembly being dimensioned for threaded engagement in said mounting cavity of said cartridge.
6. The medication delivery pen of Claim 1, wherein said pen body assembly comprises dose setting means for defining specified distances of travel for said lead screw corresponding to selected doses of medication to be delivered.
7. The medication delivery pen of Claim 1, wherein said sealed end of said cartridge comprises a pierceable elastomeric seal, and wherein said cartridge further comprises needle mounting means adjacent said distal end of said cartridge, said medication delivery pen further comprising a needle cannula assembly having a hub selectively engageable with the mounting means of said cartridge and a double-ended needle having opposed proximal and distal points, said proximal point of said needle being dimensioned and disposed to pierce said seal upon engagement with said cartridge.

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8. A reusable medication delivery pen system comprising:

a plurality of disposable cartridge holder assemblies, each said disposable cartridge holder assembly including an elongate cartridge housing having opposed proximal and distal ends, an elongate medication-containing cartridge mounted in said cartridge housing, said cartridge having a sealed distal end and an open proximal end, a plunger slidably disposed in fluid tight engagement in said cartridge, medication disposed in said cartridge intermediate said plunger and said seal, said proximal end of said housing of said cartridge holder assembly defining an array of threads;

a reusable pen body assembly having a pen body housing with opposed proximal and distal ends, said distal end of said pen body housing having an array of threads defining a pitch for threaded engagement with said threads at said proximal end of any of said cartridge housing, said pen body assembly having a driver selectively movable in proximal and distal directions in said pen body housing and dose setting means selectively adjustable for controlling amounts of movement of said driver, a lead screw having opposed proximal and distal ends, said distal end of said lead screw being selectively engageable with the plunger of any of said cartridge holder assemblies, said lead screw further comprising an array of external threads thereon threadedly engaged for rotation in said body housing, said threads on said lead screw defining a pitch substantially identical to said pitch of said threads on said distal end of said pen body housing, said lead screw being axially movable in said pen body housing in response to movement of said driver for selectively advancing said lead screw distances from said housing corresponding to selected doses of medication, whereby the substantially identical pitches of said threads on said lead screw and on said pen body housing enables said lead screw to move proximally in said body housing simultaneously with threaded engagement of said body housing with said cartridge holder housing.

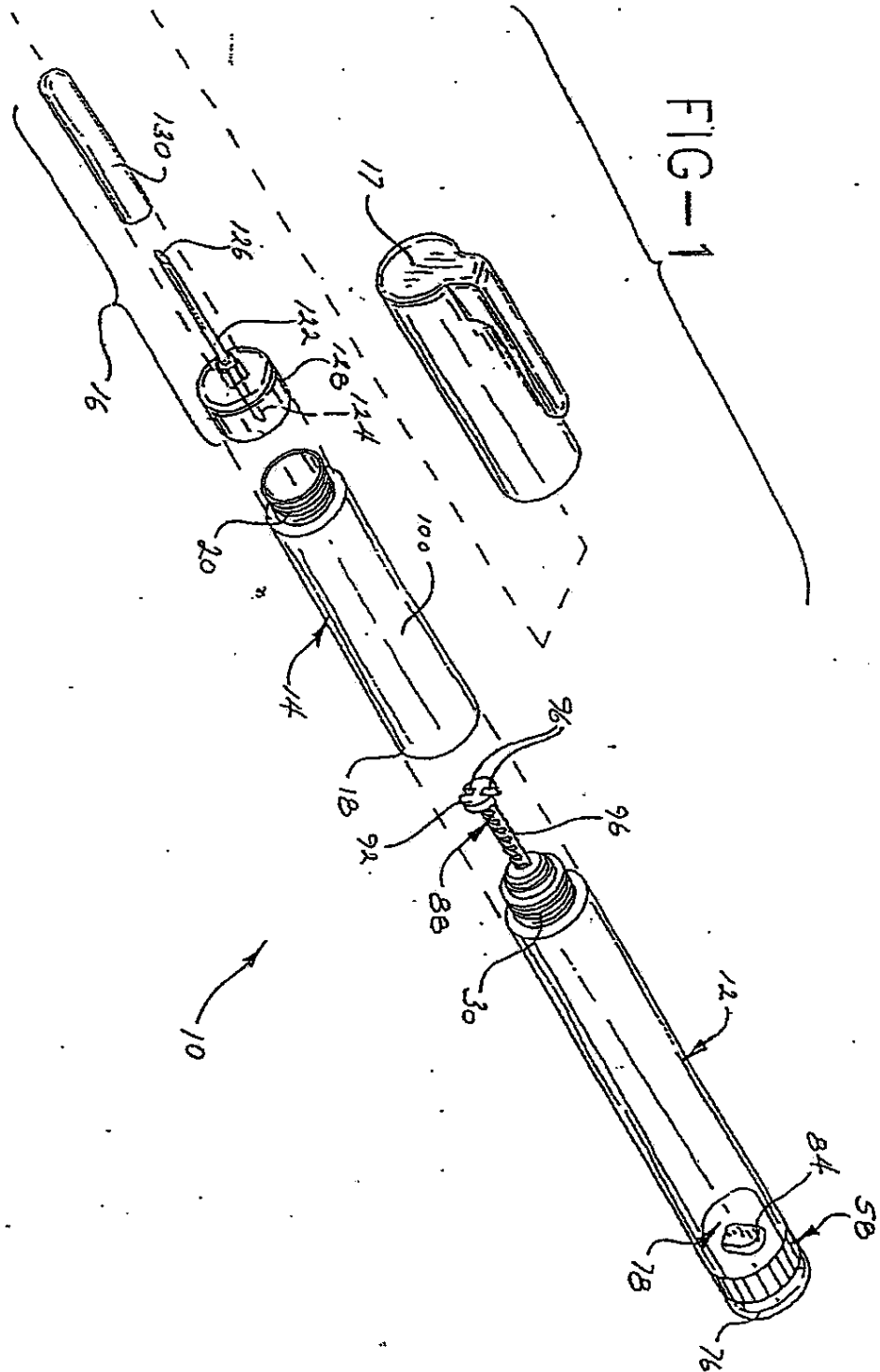
body assembly includes a longitudinally extending groove therein, and wherein each said cartridge housing includes a tab for slidably engaging the lead screw, whereby said tabs prevent relative rotation between said lead screw and said cartridge holder assembly.

9. The medication delivery pen system of Claim 8, further comprising a plurality of needle cannula assemblies, each said needle cannula assembly being selectively engageable and disengageable from each of said respective cartridge holder assemblies.

10. The medication delivery pen system of Claim 8, wherein the lead screw of said reusable pen

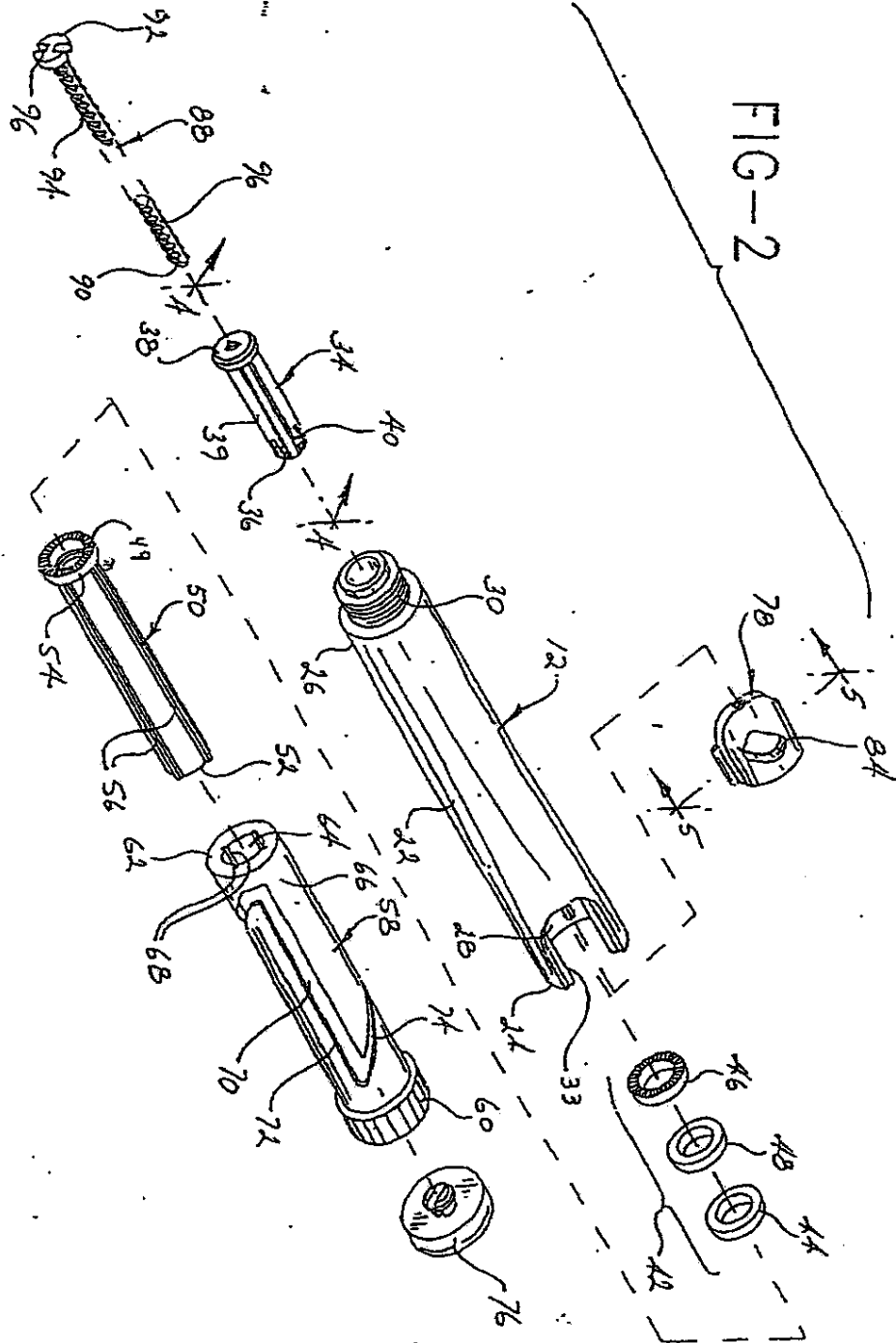
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FIG-1



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FIG-2



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FIG-3

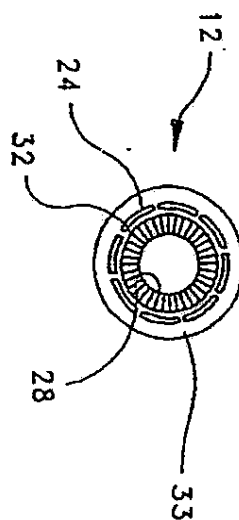


FIG-4

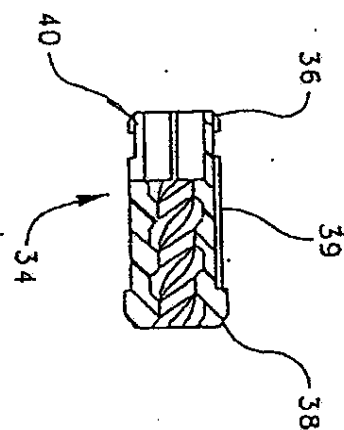


FIG-5

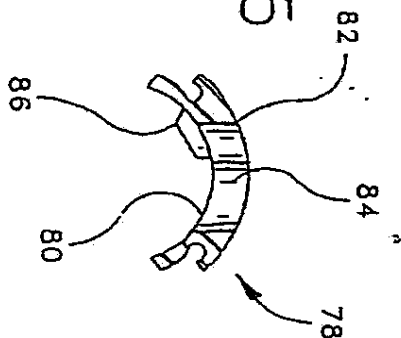
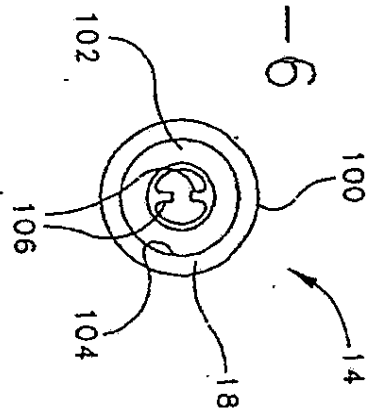


FIG-6



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FIG-7

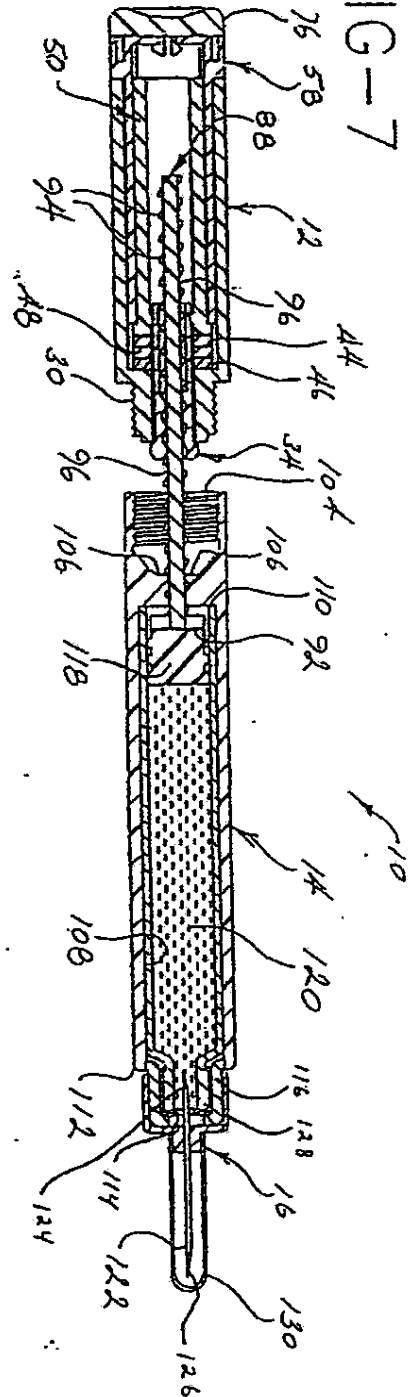
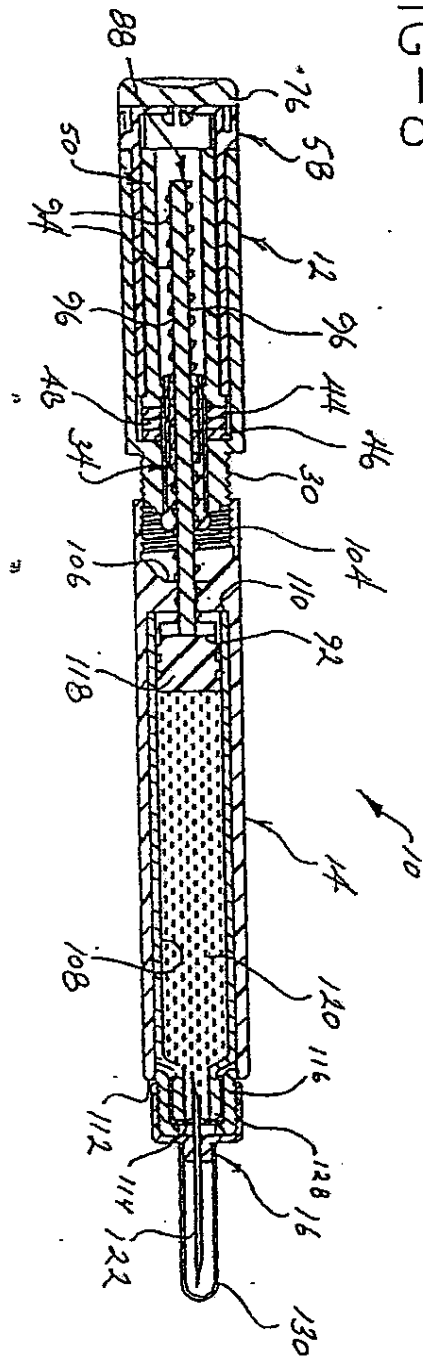


FIG-8



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FIG-9

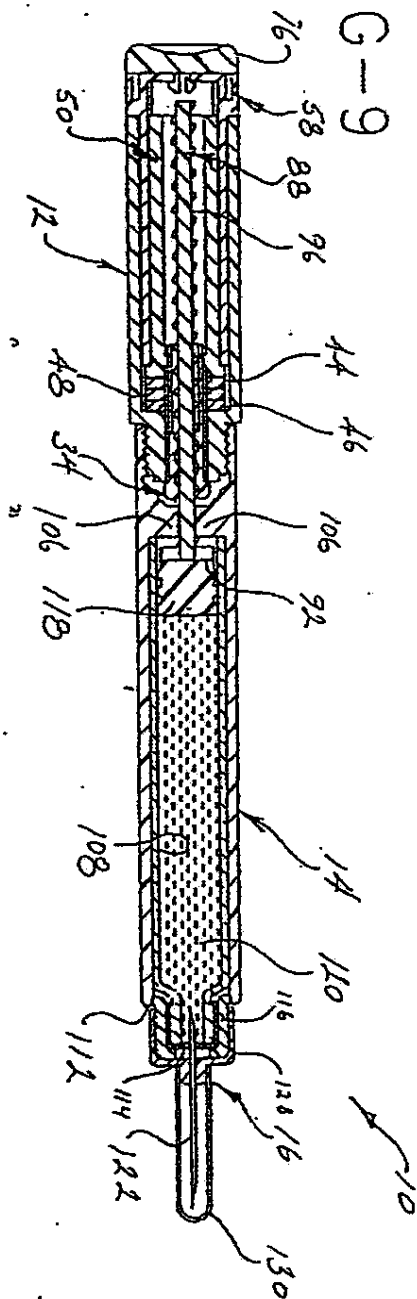
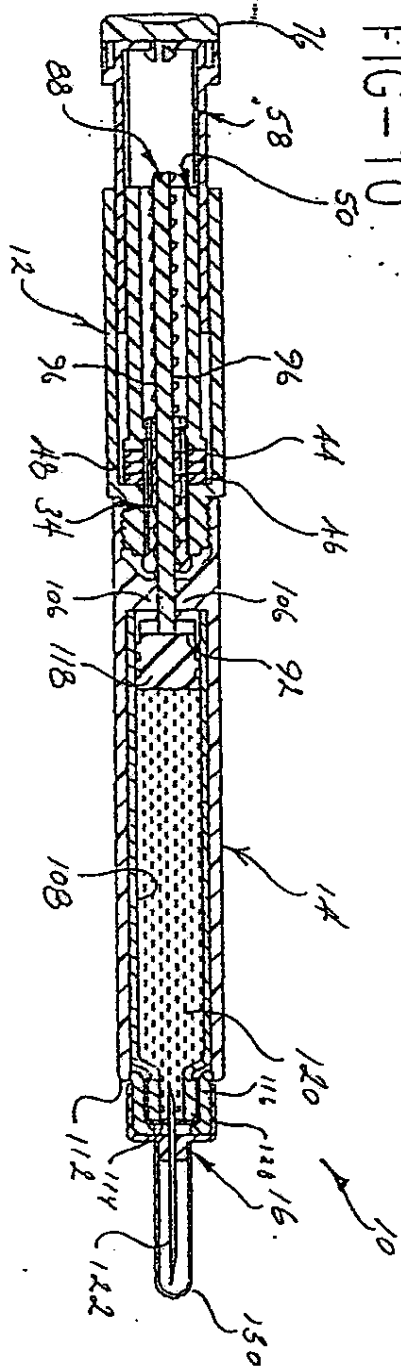


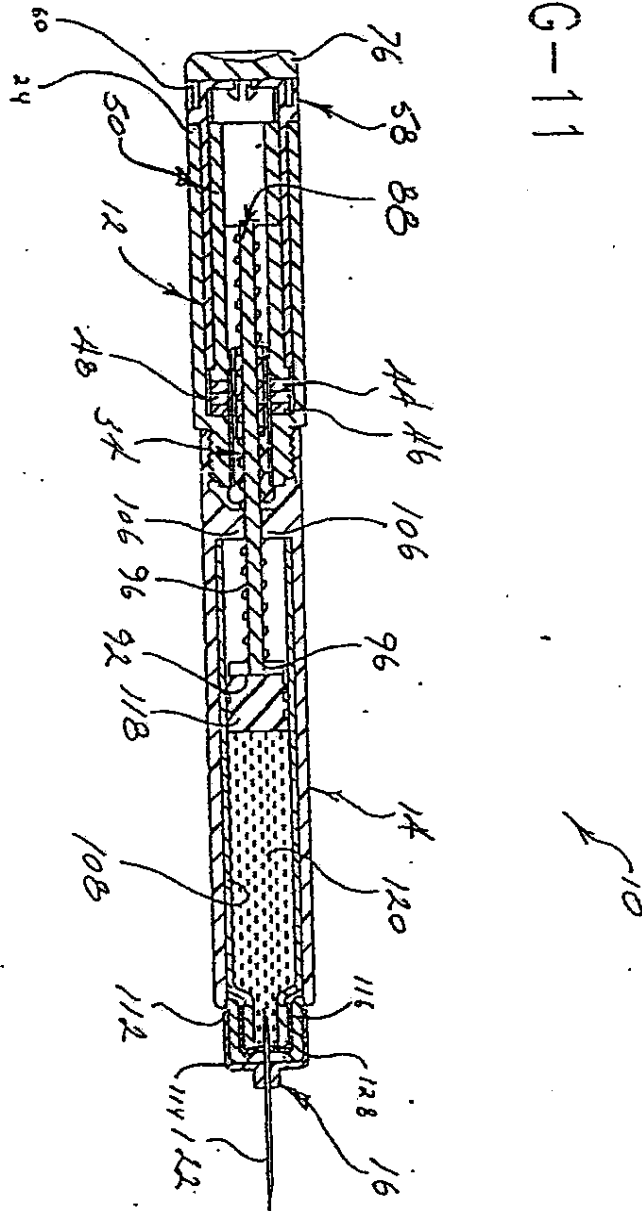
FIG-10





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FIG-11



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## EUROPEAN SEARCH REPORT

Application Number  
EP 95 30 3894

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claims	CLASSIFICATION OF THE APPLICATION (Int. Cl. 6)
X	EP-A-0 450 905 (ELI LILLY AND COMPANY) * column 2, line 19 - line 34 *	1-3, 6-10	A61M5/315
Y	* column 5, line 44 - column 6, line 13; figures 1-3, 5, 8, 9 *	5	
Y	EP-A-0 268 191 (WILHELM HASELMEIER GMBH & CO.) * figures 1-4 *	5	
A	US-A-4 973 318 (HOLM ET AL.) * abstract; figures 1-5, 13, 14, 18 *	1-10 <sup>2</sup>	
A	EP-A-0 554 995 (BECTON DICKINSON AND COMPANY)	5	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (Int. Cl. 6)
			A61M
Place of search THE HAGUE		Date of completion of the search 20 September 1995	Examiner Michels, N
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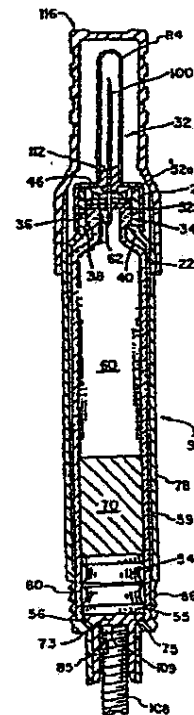
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(54) Title: CARTRIDGE ASSEMBLY FOR A LYOPHILIZED COMPOUND FORMING A DISPOSABLE PORTION OF AN INJECTOR PEN AND METHOD FOR SAME

(57) Abstract

A cartridge assembly (90) for holding a lyophilized product, forming a disposable portion of a pen injector (104), includes a cylindrical glass cartridge (58) adapted to receive the product, a closure cap (20), a cartridge case (76), and a plunger mechanism. The closure cap (20) is adapted to retain an elastomeric disc seal (52) during lyophilization and includes diametrically opposed ledges (38, 40). The closure cap (20) and seal (52) are adapted to cover a neck portion of the ampule (58), the neck portion having on its end a radially extending circumferential flange (62). The ledges (38, 40) of the closure cap (20) and the flange (62) of the neck portion allow the closure cap (20) to remain open during lyophilization, oxygen purge and nitrogen overlay. An oval-shaped indentation formed on the inside of the closure cap (20) aids in snapping the closure cap (20) about the flange (62) without crimping to retain the closure cap (20) underneath the flange (62). Reconstitution of the lyophilized drug is accomplished without foaming by use of an obliquely angled connector (30) which causes the solvent to indirectly impinge on the drug. The injection pen (104) and cartridge assembly (90) cooperate such that the length of travel of the plunger rod (108) during retraction is less than the axial length of a recess (107) in the rod tip (73).



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CARTRIDGE ASSEMBLY FOR A LYOPHILIZED COMPOUND  
FORMING A DISPOSABLE PORTION OF AN  
INJECTOR PEN AND METHOD FOR SAME

The present invention relates to the sealing and  
5 dispensing of pharmaceuticals and, more particularly to  
the sealing and dispensing of a lyophilized drug in a  
cartridge assembly.

In current technology, drugs or compounds  
manufactured for various injections are generally  
10 encapsulated in sterile glass cartridges. The glass  
cartridges characteristically have a sealed end with the  
other end of the cartridge generally having a restricted  
opening in the form of a neck having a circumferential  
flange. The opening can be closed off with a rubber  
15 membrane held into place with an aluminum seal crimped  
therearound. Where the drug or compound is to be later  
dispensed either directly from the cartridge or in a  
dispensing device such as a pen dispenser, the cartridge  
includes at the end opposite the restricted opening, an  
20 open end generally having a rubber plunger closing the  
open end. The rubber plunger also acts as a piston to  
force the drug or compound contained within the cartridge  
out of the restricted opening into which there has  
generally been inserted a cannula, by action of a plunger  
25 rod exerting axial pressure upon the rubber plunger.

Cartridges for use with dispenser devices or pens as  
described above are generally known in the prior art.  
U.S. Patent 4,936,833 Sams, shows a typical glass  
cartridge having an open end with a plunger therein, and  
30 an opposite end including a restricted opening sealed with  
a rubber membrane and crimped metal collar. The cartridge  
is insertable into a housing forming a part of a dispenser  
pen, with a cap for receiving a two ended cannula.  
Typical of these device are U.S. Patent 4,883,472 Michel,  
35 and U.S. Patent 4,973,318 Holm et al.

Lyophilized drugs or compounds are currently being  
utilized as the basis for injectionable compounds, such as

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human growth hormone (HGH), insulin, and the like.

Lyophilization is the rapid freezing of a material at a very low temperature followed by rapid dehydration by sublimation in a high vacuum. The lyophilized compound

5 is generally contained in a glass vial or cartridge. However, the process described above is not suitable for lyophilized compounds which are moisture and oxygen sensitive. When the moisture is removed from the compound during lyophilization, the oxygen in the glass cartridge  
10 containing a lyophilized drug must be replaced with nitrogen after the lyophilization process. This step of replacing the oxygen with nitrogen is termed nitrogen overlay and is accomplished within the lyophilizing chamber (freeze dryer).

15 One technique is to lyophilize the drugs or compounds in rubber stoppered glass vials. During lyophilization of the compounds in the glass vials, the rubber stopper used to close the vial is partially seated in the neck of the vial. The moisture which is removed from the compound  
20 during lyophilization is vented out through grooves or slots formed in the rubber stopper. As a general method of closing the vials, the shelves of the lyophilization chamber vertically move together to press the rubber stopper down into the vial, until the vents in the stopper  
25 are well inside the neck opening of the vial. An aluminum seal is then crimped about a flange on the neck of the vial.

The use of aluminum as a crimping seal for the rubber stopper is not, however, preferred due to the possibility  
30 of aluminum dust or particles contaminating the compound during the initial crimping, reconstitution, or administration processes. In addition, such processes as above are not well suited for efficient lyophilization.

Thus, it is desired to eliminate the aluminum  
35 crimping seal as well as provide an easier method of assuredly allowing lyophilization of a compound and sealing the same.

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In order to administer a lyophilized compound, it is necessary to reconstitute the compound prior to administration with a suitable diluent. Reconstitution is accomplished by using a syringe with a needle to withdraw the diluent from a separate vial and inject it into the vial containing the lyophilized compound. The vial containing the lyophilized compound is placed in a holder during reconstitution. Because the cartridge is filled with the lyophilized compound and nitrogen, addition of the diluent produces extra pressure within the cartridge which creates the possibility of forcing the plunger out of the cartridge. Having the plunger forced out of the cartridge during reconstitution would undesirably result in a total loss of the compound.

During reconstitution, the diluent injected from the syringe into the cartridge directly impinges upon the lyophilized compound which causes the lyophilized compound to foam. The foam undesirably creates extra head space within the cartridge such that the proper amount of diluent is not mixed with the compound, resulting in an improper diluent to compound ratio. In order to alleviate this, one must wait for the foam to subside.

A patient needle is then attached to the disc sealed end of the cartridge which thus allows the compound to be injected. Current injector pens dispense a selectable amount of drug depending on the required dosage. A plunger mechanism, including a plunger rod, pushes against the plunger in the cartridge. After each injection, the plunger mechanism and plunger rod retract during a resetting function of the injector pen. However, complete disengagement of the plunger rod from the plunger mechanism during retraction is highly undesirable, and can render the injector pen inoperative.

Because of the expanding use of pen dispensers or injectors utilizing cartridges for the administration of injectionable compounds, it is desired to provide a

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lyophilized compound in an improved cartridge suitable for use in an injector pen.

The present invention, in one form thereof, provides a method of lyophilizing a compound in a glass cartridge and sealing the same utilizing a closure cap with a seal, and encapsulating the same into a cartridge assembly.

A method of lyophilizing and sealing an injectionable product within a cartridge is provided which includes, providing a cartridge having a neck defining a first opening therein, and a second opening therein distal the first opening, the neck including a circumferential radially outwardly extending flange adjacent the first opening, inserting a plunger in the second opening, and inserting the product to be lyophilized into the cartridge. Further, there is provided a cap having a cylindrical portion and a seal, the cylindrical portion including an open bottom receivable over the neck, the cap including a top having an opening therein for receipt of a needle therethrough, at least one vent circumferentially disposed in the cap, and a deformable ledge in the cap extending radially inwardly from the cylindrical portion axially below the vent, the seal being axially disposed between the vent and the top so as to block the top opening. The cap is then placed onto the neck such that the deformable ledge rests upon the neck flange and the vent is in communication with the neck opening, after which the cartridge with the cap is placed in a lyophilizing chamber, wherein the product is lyophilized, and the cap is closed by exerting a downward pressure upon the cap such that the deformable ledge yieldably snaps around the neck flange to be lockingly retained thereunder, the vent is closed from communication with the neck opening, and the seal is compressed into sealing engagement with the neck opening by downward pressure exerted by the top thereby providing an air impermeable barrier between the top opening and the neck opening.

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The method of sealing a lyophilized product within a cartridge is further characterized by providing a sleeve having a first open end and a radially inwardly extending circumferential ledge into which the cartridge is placed.

5 The cartridge is axially seated against the ledge and the sleeve is permanently attached to the cap.

A plunger rod tip having a plunger head is received in the sleeve between the plunger and ledge such that the plunger head is axially adjacent the plunger.

10 The present invention, in one form thereof, provides a cartridge assembly containing a lyophilized drug having a cartridge, a cap and seal, a cartridge sleeve, and a plunger mechanism forming a disposable portion of an injector pen.

15 A cartridge assembly for holding a lyophilized drug and forming a disposable part of an injection pen comprises a cartridge having a plug in one end and a neck on another end, the cartridge including a circumferentially extending flange about the neck, the  
20 neck defining an opening therein, a cap disposed about the neck, the cap having a first cylindrical portion including an open bottom received over the neck, a top having an opening therein for receipt of a needle therethrough, and a deformable ledge extending radially inwardly from the  
25 first cylindrical portion and lockingly retained under the neck flange. A resilient seal is disposed in the cap between the neck opening and the top opening forming an impermeable barrier therebetween, with a sleeve radially disposed about and permanently attached to the cartridge.

30 Further, the sleeve is permanently attached to the cap, and includes a first cylindrical portion adapted to receive the cartridge and a second cylindrical portion axially below the first cylindrical portion and concentric therewith, and a radially inward circumferentially  
35 extending ledge defined at the junction of the first and second cylinder for axially retaining the one end of the cartridge.

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In one form thereof the present invention provides a method and apparatus for reconstituting a lyophilized compound, the lyophilized compound contained within an interior space defined by an inner wall of the cartridge having an inlet at one end thereof. The method comprising the step of injecting a diluent into the cartridge via the inlet such that the diluent impinges on and runs down the inner wall of the cartridge to thereby contact the compound, whereby foaming of the compound is alleviated.

10 A connector is releasably secured to the inlet end of the cartridge and adapted to receive and hold a syringe containing a diluent. The connector has a first portion defining a longitudinal axis which forms an oblique angle with the longitudinal axis of the cartridge. The syringe is supported by the connector at the oblique angle whereby the diluent is injected into the cartridge via the inlet at the oblique angle so that the diluent impinges on the wall of the cartridge.

The cartridge of the present invention is adapted to be used with an injector pen apparatus for administering a drug. The apparatus comprises a cartridge assembly having a cartridge with a movable plunger therein and an inlet on one end thereof. The cartridge assembly includes a rod tip having a recess therein and disposed axially adjacent the plunger and is adapted to exert pressure upon the plunger for dispensing the drug from the cartridge. An injector pen is releasably engaged with the cartridge assembly, the pen including a movable rod adapted to engage the recess of the rod tip in order to move the rod tip during dispensing of the drug. For injection of the drug, the rod retracts a known distance away from the plunger within the recess of the rod tip. The rod is then advanced towards the plunger a selected number of discrete increments as determined by the number of clicks depending on the desired dosage to be administered. During injection, the rod then advances the known distance towards the plunger which causes the plunger to advance

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the distance determined by the amount of discrete increments. The rod then retracts the known distance within the travel length of the rod tip.

It is an advantage of the present invention that the  
5 closure cap does not require close tolerances in cartridge manufacture.

It is another advantage of the present invention in that the cartridge, closure cap with seal, and cartridge case with plunger form a tamper resistant package.

10 It is yet another advantage of the present invention that the cartridge assembly prevents the plunger from outwardly moving during shipment of the cartridge assembly and during reconstitution of the lyophilized drug contained therein.

15 It is further an advantage of the present invention that foaming of the lyophilized compound is prevented during reconstitution thereof.

It is still another advantage of the present invention in that the cartridge assembly is protected from  
20 breakage.

It is also an advantage of the present invention that container integrity for the drug is increased.

The above mentioned and other features and objects of this invention, and the manner of attaining them, will  
25 become more apparent and the invention itself will be better understood by reference to the following description of embodiments of the invention taken in conjunction with the accompanying drawings, wherein:

Fig. 1A is a perspective view of the closure cap  
30 according to an aspect of the present invention;

Fig. 1B is a bottom view of the closure cap taken along line 1B-1B of Fig. 2;

Fig. 2 is a sectional elevational view of the closure cap taken along line 2-2 of Fig. 1A;

35 Fig. 3 is an elevational cutaway view of the glass cartridge and plunger;

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Fig. 4 is an elevational cutaway view of the glass cartridge with plunger seated on a shelf with the closure cap in an open condition;

Fig. 5 is an elevational cutaway view of the glass cartridge with plunger seated on a shelf with the closure cap in a closed position;

Fig. 6 is an elevational cutaway view of a cartridge assembly with user needle and cap;

Fig. 7 is an elevational cutaway view of the cartridge assembly according to an embodiment of the present invention;

Fig. 8 is a partial cutaway view of the cartridge assembly according to an embodiment of the present invention installed on a dispensing pen unit;

Fig. 9 is an elevational cutaway view of the cartridge assembly during reconstitution;

Fig. 10 is an elevational cutaway view of the cartridge assembly with connector and connector lid before insertion into a dispensing pen and reconstitution;

Fig. 11 is a partial cutaway view of the cartridge assembly installed on a dispensing pen; and

Figs. 12-14 are partial cutaway views of the plunger and rod mechanism as utilized with the dispensing pen illustrating the injection process.

Corresponding reference characters indicate corresponding parts throughout the several views. The exemplifications set out herein illustrate a preferred embodiment of the invention, in one form thereof, and such exemplifications are not to be construed as limiting the scope of the invention in any manner.

Referring now to Figs. 1A, 1B, and 2, there is shown a closure or lyophilization cap 20 in accordance with an aspect of the present invention. In general, cap 20 is preferably made of an injection molded plastic, although other suitable materials as known in the art may be utilized with the cap thus fabricated accordingly. Cap 20 has a cylindrical bottom portion or skirt 22 of a given

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axial length and inner radius sufficient to extend about at least a portion of a lyophilization cartridge. As further described hereinbelow, bottom portion or skirt 22 stabilizes cap 20 when placed onto cartridge 58 in the open position during lyophilization, and serves as a guide during closing of the cap. Cylindrical bottom portion 22 has a slightly upwardly and inwardly sloping annular shoulder 24, with a cylindrical top portion or neck 26 disposed axially above and inwardly concentric to cylindrical bottom portion 22. Top portion 26 includes threads 28 circumferentially formed on the outer upper periphery thereof which are adapted to threadedly receive a connector 30 (Figs. 9 and 10) and needle assembly 32 (Fig. 6) both of which are described in more detail hereinbelow. Formed in cylindrical top portion 26 below threads 28 are two diametrically opposed circumferentially extending rectangular openings 34 and 36 which serve to vent moisture from cartridge 58 (Figs. 3-5) during lyophilization and which allow the oxygen purge and nitrogen overlay process to occur thereafter.

As best seen in Fig. 1B, extending radially inward from wall 33 and 35 just below openings 34 and 36 are two ledges 38 and 40 having a circumferential length roughly corresponding to openings 34 and 36. As will be described in more detail hereinbelow, ledges 34 and 36 serve the dual function of allowing closure cap 20 to be seated upon cartridge 58 thus permitting communication between openings 34, 36 and the interior 60 of cartridge 58, and of snapping around and under circumferential flange 62 of cartridge neck 64 upon closing cap 20. Ledges 38 and 40 are sized and shaped so as to reduce the closing pressure required during the closing process, described hereinbelow, and to minimize the amount of cap deformation as closure is taking place. Cap 20 includes a top 41 which downwardly slopes from the outer upper edge of cylindrical top portion 26 terminating at an aperture 46 adapted to expose a seal 52 and receive a needle as

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described in detail hereinbelow. Two arched slots 42 and 44 are disposed in top portion 41 each axially upwardly of a respective side opening 34, 36. Arched slots 42 and 44 are formed during the molding process in order to achieve the undercut ledges 38 and 40 sufficiently large enough to allow for variations in the diameters of cartridge flanges.

Defined at the level 50 of ledges 38, 40 interior to cap 20 are walls 33, 35, 47, and 48 that define an oval or elliptic surface 49 whose major axis is transverse to an axis defined by connecting the middle of side openings 34, 36 or ledges 38, 40 such that each longitudinal end of oval or ellipse 49 is located 90° from each ledge 38 and 40. Walls 47 and 48 are thinner than walls 33 and 35 carrying ledge 38 and 40 so that as the ledges are forced outwardly during seating of cap 20, walls 47, 48 can move inward to accommodate such outward movement of walls 33 and 35 carrying ledges 38, 40. However, the thicker walls 33, 35 provide adequate support for ledges 38, 40 to prevent dislodgement of cap 20 from cartridge 58. This reduces the pressure required to close cap 20 onto cartridge 58 after lyophilization and nitrogen purge in order to prevent stress fractures in cap 20 and allow for more cartridges to be closed at one time. Such elliptical configuration of walls 33, 35, 47 and 48 extends the entire inner axial length thereof.

A circumferential ridge 51 is disposed about the interior of cylindrical top portion 26 axially below and adjacent top 41. Ridge 51 permits seal 52, such as for instance a laminated, two-piece rubber seal, to be seated therein without dislodging for efficient covering of opening 46.

The structure of cap 20 assists the natural deformation that occurs during the closure process. Thus, as cap 20 is pressed onto cartridge 58, ledges 38, 40 spring outward to allow it to go over and then underneath neck flange 62 (see Fig. 3).

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What has thus been described hereinabove is a cap adapted to be seated upon a cartridge during lyophilization and which effectively and positively closes upon the cartridge to securely hold a disc seal about the opening.- The cap is designed for efficient lyophilization and optimal nitrogen sealability while requiring only a minimum amount of closure force.

The process of lyophilizing a compound in cartridge 58 utilizing the hereinabove described cap 20 will now be described in conjunction with Figs. 3-5. First, it should be noted that the various parts are sterilized prior to placement in the freeze dryer so that the compound to be lyophilized will be free from contamination. Secondly, it should be noted that a plurality of cartridges (up to 6000 or more) are generally lyophilized at one time. The cartridges are held in blocks defining a matrix of rows and columns of cartridges with the blocks placed in a freeze dryer chamber between movable shelf units, described hereinbelow. A typical configuration is 2000 per layer with three layers. The general structure of the various elements will also be described when introduced during the description of the process.

Cartridge 58 is manufactured of glass and consists of a tube portion 59 defining an inner chamber 60 and which openly terminates at one end with a circumferential inwardly bulbous lip 56. The other end of tube 59 includes an upwardly and inwardly sloping shoulder portion 66, a reduced diameter neck 64 and a rim 63 having circumferential flange 62 having a circumferential radius greater than that of neck 64. The end of cartridge 58 including flange 62 defines an opening 68 which communicates with inner chamber 60. Recessed neck 64 has a diameter that is smaller than shoulder 66. A rubber plunger 54 having knobs 55 is first disposed in the end having lip 56 just far enough into cartridge 58 such that the end of plunger 54 is adjacent lip 56. This is to keep the inside of cartridge 58 sterile after lyophilization.

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Cartridge 58 with plunger 54 is placed between shelves 72 and 74 in the freeze dryer (not shown) with the liquid compound or drug 70 to be lyophilized contained therein. Cap 20 having rubber disc seal 52 disposed  
5 therein is placed over flange 62 defining a first or open position, the placement of cap 20 onto cartridge 58 occurring either before placement of cartridge 58 into the freeze dryer or thereafter. However, compound 70 is placed into cartridge 58 before the placement of cap 20  
10 upon flange 62. Seal 52 is preferably a laminate of two different materials, the upper material 52a being a good sealing material, with the bottom material 52b being a good product contact material such as, for example, a normal butyl rubber compound. However, any resilient  
15 sealing material may be utilized which provides a good product contact material on the bottom and a good sealing material on the top.

Referring specifically to Fig. 4, cap 20 is designed such that ledges 38 and 40 rest on top of flange 62. In  
20 the first or open position a part of cylindrical bottom portion 22 circumferentially surrounds an upper part of tube 59 thereby serving as a stabilizer for cap 20 and a guide when cap 20 is moved to the second or closed position. Seal 52 is held in an elevated position above  
25 cartridge opening 68, while side openings 34 and 36 are above opening 68 thus allowing communication between the ambient atmosphere and inner chamber 60 of cartridge 58. At this point lyophilization begins.

Lyophilization, or freeze drying, which is  
30 represented in Fig. 4 as an upward and outward arrow, purges the moisture from compound 70 such that a waterless compound is left. Although the arrow is shown exiting only one side opening 36, it should be understood that the moisture is vented out through both openings 34, 36 during  
35 lyophilization. Once the moisture has been vented out of cartridge 58, oxygen is purged from the lyophilization chamber and thus cartridge 58. A nitrogen overlay process

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is then initiated. The nitrogen overlay process is represented in Fig. 4 as an inward and downward arrow entering from side opening 34, but as is the case for the venting of moisture and oxygen purge, the nitrogen enters through both side openings 34 and 36 to fill the entire inner space 60 of cartridge 58 not occupied by the now lyophilized compound 70. The nitrogen overlay process is used where the lyophilized compound is oxygen sensitive, as, for example, HGH.

At this point and referring now to Fig. 5, shelves 72 and 74 move vertically together in order to close cap 20 onto neck 64. As described above, cap 20 includes an oval or elliptical indentation 47 and inner wall 48 which allows cap 20 and ledges 38 and 40 to deform and flex so that ledges 38 and 40 snap around flange 62 as cap 20 is downwardly pressed by the pressure exerted by closing shelves 72 and 74. A force of only about 10-12 lbs. is thus necessary to effect closure of cap 20 about neck 64 and neck flange 62. Once in place, cylindrical bottom portion 22 extends about an upper part of tube 59, while ledges 38 and 40 prohibits removal of cap 20 by extending under neck flange 62 between the flange and sloped shoulder section 66.

Upon closure of cap 20, seal 52 is compressed between the top of rim and downwardly sloped cap top 41 to effect a positive, airtight seal between the ambient atmosphere and the nitrogen and lyophilized compound within cartridge 58. There is no need for a crimp seal, while both the lyophilization and closure processes are completed within the lyophilizing chamber. At this point, the sealed cartridge may be removed from the lyophilizing chamber. A cake or plug of compound 70 is thus sealed within a nitrogen filled cartridge.

After lyophilization, and referring to Fig. 7, sealed cartridge 58 is then placed into a cartridge sleeve, barrel, or retainer 76 through an opening 77 in one end thereof. The sleeve is preferably made from a suitable

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plastic or other material which provides protection for the glass cartridge.

Sleeve 76 comprises a first tubular portion 78 having an inner diameter 79 of sufficient size such that a  
5 segment of first tubular portion 78 radially surrounds or overlaps cylindrical bottom portion 22 of cap 20. At this junction, sleeve 76 is attached or sealed to cap 20 by use of a solvent, adhesive bond, snap fit, sonic weld, or the like, such that cartridge 58 is retainingly held in sleeve  
10 76. Sleeve 76 also includes a second tubular portion 80 having a smaller diameter than first tubular portion 78 such that tube 59 of cartridge 58 is inwardly circumjacent the inner diameter thereof. Threads 86 on the outer periphery of second tubular portion 80 permit sleeve 76 to  
15 be received onto an injection pen device.

Sleeve 76 further comprises a third tubular portion 82 having a smaller diameter than second tubular portion 80, the second tubular portion defining an annular stop or ledge 84 at the junction of second and third tubular  
20 portions 80 and 82. Stop 84 supports lip 56 such that tube 59 is supported thereon. A sleeve cap 88 optionally may fit about the top of the cartridge assembly 90 to further protect the seal assembly. Thus, the cartridge is securely held by and contained within sleeve 76 and ready  
25 for reconstitution before administration and placement into an injector pen dispenser.

Sleeve 76 has a smaller diameter opening 69 at the other end through which extends a plunger rod tip 71. Rod tip 71 is placed within sleeve 76 before insertion of  
30 cartridge 58, and has a circular rod head 73, slightly less than the inner diameter of cartridge 58, on one end of a hollow cylindrical body 85. The lower portion of rod head 73 is seated against sleeve ledge 84 and is of sufficient diameter such that rod tip 71 is retained in  
35 sleeve 76. Rod tip body 85 is of sufficient length to axially extend from head 73 to the axial end of third tubular portion 82. Cylindrical body 85 defines an

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axially elongated cylindrical recess or bore 107. Recess 107 defined by cylindrical body 85 between bottom portion 81 of rod head 73 and end portion 83 is of a specific axial length, for example, eight and nine tenths  
5 millimeters (8.9 mm). The upper surface of circular rod head 73 of rod tip 71 abuts plunger 54 and includes an annular groove 75 into which knobs 55 of plunger 54 are seated. As pressure is applied to plunger 54 in order to administer the reconstituted compound, plunger 54, being  
10 an elastomeric or rubber, has a tendency to deform during compression. However, because of its resiliency, plunger 54 returns to its original shape, which sequence could cause weeping of the liquid from around the plunger. Rod head 73 serves to distribute the load exerted by the  
15 compression of rod tip 71 in order to eliminate weeping from about plunger 54 which could occur as a result of uneven or localized compression of plunger 54. Annular groove 75 retains knobs 55 to prevent lateral deformation, which could cause weeping.

20 As shown in Fig. 10, a connector 30 is threadedly attached to threads 28 of cap 20. This occurs after placement of cartridge 58 in sleeve 76 and attachment of cap 20 thereto. Connector 30, introduced hereinabove, is threadedly attached to threads 28 of cap 20 and includes  
25 an angled first section 92 and a larger diameter second section 94. First section 92 is tubular in shape and includes an upper section 111 and, at its lower end, an angled neck portion 113 having mating threads for threads 28. Neck portion 113 is essentially concentric and  
30 defines a common axis with cartridge 58. Upper section 111 defines an axis which thus forms an oblique angle with the axis of neck portion 113. Larger diameter portion 94 is eccentric with upper section 111 of first section 92. A common axis is also defined between upper section 111  
35 and portion 94.

A lid 95 is snapped in place over cylindrical second section 94 thereby sealing the space there between. This

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entire assembly is then sterilized so that the contents of the cartridge and the area about the disc seal is sterile for later reconstitution and administration.

Reconstitution is performed as shown in Fig. 9.

- 5 After removal of connector lid 95, connector 30 is thus adapted to receive a syringe 96 in second section 94 which supports syringe 96 but allows needle 98 to enter hole 46 and penetrate seal 52 such that only a small section of needle 98 extends into cartridge 58. During
- 10 reconstitution, the action produced by the force of moving diluent upon the lyophilized cake (e.g. HGH) triggers a reaction which causes the HGH cake to become agitated and foam. Foaming undesirably creates air bubbles, thereby limiting the amount of diluent that can be added to the
- 15 cartridge. This can result in improper dilution ratios of the lyophilized compound. Furthermore, once the foam subsides, too large a headspace is created within the cartridge.

- According to one aspect of the present invention,
- 20 connector 30 is obliquely angled as described above such that needle 98 is oriented toward and preferably in close proximity to wall 58 and injects diluent 102 down the side of the interior wall of cartridge 58 in order to prevent foaming of the compound during the reconstitution process.
- 25 Side impingement of the diluent reduces the velocity of the diluent as it travels toward and onto the HGH cake. This indirect administration of the diluent by causing the diluent to impinge on the inner side wall of cartridge 58 and then run down around and into the HGH prevents
- 30 foaming.

- Syringe 96 is prefilled with a suitable diluent 102, and as plunger 100 of syringe 96 forces fluid into the lyophilized cartridge, the nitrogen in cartridge 58 is compressed. Releasing syringe plunger rod 100 while
- 35 holding the syringe above the cartridge, allows the pressure in the cartridge to equilibrate by venting the nitrogen into the syringe, leaving the diluent in the